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NEWS 6 Oct 27 Plasmid Key Serials Dictionary and Echoing added to
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=> s MJ? and TCR and (RTPCR or PCR)
L1 0 MJ? AND TCR AND (RTPCR OR PCR)

=> s MJ? and alpha
L2 0 MJ? AND ALPHA

=> MJ? and TCR
MJ? IS NOT A RECOGNIZED COMMAND
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=> s MJ? and TCR
L3 6 MJ? AND TCR

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4 3 DUP REM L3 (3 DUPLICATES REMOVED)

=> dis l4 1-3 ibib abs kwic

L4 ANSWER 1 OF 3 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1998313352 MEDLINE
DOCUMENT NUMBER: 98313352
TITLE: Energy of adhesion of human T cells to adsorption layers of
monoclonal antibodies measured by a film trapping
technique.
AUTHOR: Ivanov I B; Hadjiiski A; Denkov N D; Gurkov T D;
Kralchevsky P A; Koyasu S
CORPORATE SOURCE: Laboratory of Thermodynamics and Physico-chemical
Hydrodynamics, Faculty of Chemistry, University of Sofia,
1126 Sofia, Bulgaria.
SOURCE: BIOPHYSICAL JOURNAL, (1998 Jul) 75 (1) 545-56.
Journal code: A5S. ISSN: 0006-3495.
PUB. COUNTRY: United States
LANGUAGE: Journal; Article; (JOURNAL ARTICLE)
English

W0 9807870
19980226

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY WEEK: 19981003

AB A novel method for studying the interaction of biological cells with interfaces (e.g., adsorption monolayers of antibodies) is developed. The method is called the film trapping technique because the cell is trapped within an aqueous film of equilibrium thickness smaller than the cell diameter. A liquid film of uneven thickness is formed around the trapped cell. When observed in reflected monochromatic light, this film exhibits an interference pattern of concentric bright and dark fringes. From the radii of the fringes one can restore the shape of interfaces and the cell. Furthermore, one can calculate the adhesive energy between the cell membrane and the aqueous film surface (which is covered by a layer of adsorbed proteins and/or specific ligands), as well as the disjoining pressure, representing the force of interaction per unit area of the latter film. The method is applied to two human T cell lines: Jurkat and its T cell receptor negative (TCR-) derivative. The interaction of these cells with monolayers of three different monoclonal antibodies adsorbed at a water-air interface is studied. The results show that the adhesive energy is considerable (above 0.5 mJ/m²) when the adsorption monolayer contains antibodies acting as specific ligands for the receptors expressed on the cell surface. In contrast, the adhesive energy is close to zero in the absence of such a specific ligand-receptor interaction. In principle, the method can be applied to the study of the interaction of a variety of biological cells (B cells, natural killer cells, red blood cells, etc.) with adsorption monolayers of various biologically active molecules. In particular, film trapping provides a tool for the gentle micromanipulation of cells and for monitoring of processes (say the activation of a T lymphocyte) occurring at the single-cell level.

AB . . . the latter film. The method is applied to two human T cell lines: Jurkat and its T cell receptor negative (TCR-) derivative. The interaction of these cells with monolayers of three different monoclonal antibodies adsorbed at a water-air interface is studied. The results show that the adhesive energy is considerable (above 0.5 mJ/m²) when the adsorption monolayer contains antibodies acting as specific ligands for the receptors expressed on the cell surface. In contrast, . . .

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1996:588743 CAPLUS
DOCUMENT NUMBER: 125:212708
TITLE: Receptor fusion proteins and chimeric genes encoding them and their use in the control of proliferation in the treatment of disease
INVENTOR(S): Capon, Daniel J.; Tian, Huan; Smith, Douglas H.; Winslow, Genine A.; Siekevitz, Miriam
PATENT ASSIGNEE(S): Cell Genesys, Inc., USA
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9623881	A1	19960808	WO 1996-US1292	19960202
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, UZ, VN, AZ, BY, KG, KZ				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5741899	A	19980421	US 1995-481003	19950607
US 5837544	A	19981117	US 1995-485293	19950607
US 6077947	A	20000620	US 1995-485598	19950607
CA 2221634	AA	19960808	CA 1996-2221634	19960202
AU 9648612	A1	19960821	AU 1996-48612	19960202
AU 715363	B2	20000203		
EP 821730	A1	19980204	EP 1996-904532	19960202
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
PRIORITY APPLN. INFO.: US 1995-382846 19950202				
WO 1996-US1292 19960202				

AB Chimeric receptors for proliferation-stimulating effectors are described for use in the treatment of disease (cancer, infectious, or autoimmune disease). The receptors are made up of combinations of domains from known receptors. One group has an extracellular clustering domain (ECD), transmembrane domain (TM), proliferation signaling domain (PSD) that can signal a host cell to divide. A second group has an intracellular clustering domain (ICD) and a proliferation signaling domain (PSD) that can signal a host cell to divide. A third group has an extracellular clustering domain (ECD) or an intracellular clustering domain (ICD), a transmembrane domain (TM), proliferation signaling domain (PSD), and an effector signaling domain that can signal an effector function and a host cell to divide. Chimeric genes for these receptors and methods for their expression and the therapeutic uses of the receptors and genes are described. The prepn. of fusion proteins of the ligand receptor and extracellular clustering domains of CD4 and Janus kinase or cytokine receptor subunits are described.

IT Plasmid and Episome
(pIKCD4-FKBP-mJAK1, chimeric gene for FK506-binding protein fusion with CD4 antigen and JAK1 kinase on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKCD4-FKBP-mJAK2, chimeric gene for FK506-binding protein fusion with CD4 antigen and JAK2 kinase on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKCD4-FKBP-mJAK3, chimeric gene for FK506-binding protein fusion with CD4 antigen and JAK3 kinase on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKCD4-Syk-mJAK1, chimeric gene for CD4 antigen .zeta. subunit fusion product with Syk and JAK1 kinases on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKCD4-Syk-mJAK2, chimeric gene for CD4 antigen .zeta. subunit fusion product with Syk and JAK2 kinases on; receptor fusion

[illegible]

Receptors

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TCR (T-cell antigen receptor), fusion products; receptor
fusion proteins and chimeric genes encoding them and their use in
control of proliferation in treatment of disease)

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1990:542927 CAPLUS
DOCUMENT NUMBER: 113:142927
TITLE: Electron transport properties of thermodynamically
stable aluminum-copper-ruthenium icosahedral
quasicrystals
AUTHOR(S): Mizutani, U.; Sakabe, Y.; Shibuya, T.; Kishi, K.;
Kimura, K.; Takeuchi, S.
CORPORATE SOURCE: Dep. Cryst. Mater. Sci., Nagoya Univ., Nagoya, 464-01,
Japan
SOURCE: J. Phys.: Condens. Matter (1990), 2(28), 6169-78
CODEN: JCOMEL
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The electron transport properties of the thermodynamically stable
Al₆₈Cu₁₇Ru₁₅ quasicrystal were studied through the measurements of the
electronic sp. heat coeff. and the temp. dependence of the elec.
resistivity at 4.2-300 K. The full-width at the half max. for the
strongest x-ray diffraction line (100000) is reduced to <0.15 nm⁻¹ either
by remelting the ingot with subsequent furnace cooling or by annealing the
melt-spun ribbon at 850.degree. for 24 h. An apparent improvement in
quasi-crystallinity upon the heat-treatment caused a drastic increase in
resistivity up to 1600 .mu..OMEGA. cm and accompanied a very small
electronic sp. heat coeff. .gamma. lower than 0.3 mJ mol⁻¹ K⁻².
The temp. dependence of the resistivity characterized by a concave
curvature with a neg. TCR can be discussed in terms of the weak
localization of conduction electrons. The thermodynamically stable
quasicrystals, like the present Al-Cu-Ru and the previously studied
Al-Li-Cu, always exhibit a very low .gamma. value coupled with a high
resistivity. The electron d. of states in thermodynamically stable
quasicrystal may possess a structure-induced min., and the Fermi level
does fall in this crit. range. An increase in the resistivity upon
improvement in quasi-crystallinity is discussed in terms of the
generalized Faber-Ziman theory and in terms of a possible enhancement in
the coherent multiple scattering due to locally well-developed short-range
order.

AB The electron transport properties of the thermodynamically stable
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quasicrystal may possess a structure-induced min., and the Fermi level
does fall in this crit. range. An increase in the resistivity upon
improvement in quasi-crystallinity is discussed in terms of the
generalized Faber-Ziman theory and in terms of a possible enhancement in
the coherent multiple scattering due to locally well-developed short-range
order.

=> s tcr and rtprcr and (J? or M?)

TERM 'M?' EXCEEDED TRUNCATION LIMITS - SEARCH ENDED

<-----User Break----->

u

SEARCH ENDED BY USER

SEARCH ENDED BY USER

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Make the stem longer and try again. For example, if your original
term was 'degr?' to search for variations and the abbreviation for
'degradation', you could replace it with the expression '(degrdn OR
degrad?)'. If your search term was numeric, e.g., 'C>5', reduce the
size of the range.

=> s tcr and rtprcr and oligo?

L5 1 TCR AND RTPCR AND OLIGO?

=> dis 15 ibib abs kwic

L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1997:697109 CAPLUS
DOCUMENT NUMBER: 127:342368
TITLE: Complementary anchor PCR of rearranged variable T-cell
receptor .beta.-chain cDNA regions
AUTHOR(S): Oduncu, F.; Krause, G.; Rohnisch, T.; Emmerich, B.;
Pachmann, K.
CORPORATE SOURCE: Medizinische Klinik, Klinikum Innenstadt, Munich,
D-80336, Germany
SOURCE: Biol. Chem. (1997), 378(10), 1211-1214
CODEN: BICHF3; ISSN: 1431-6730
PUBLISHER: de Gruyter
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Sequencible amplicates comprising the variable cDNA sequences of the
rearranged T-cell receptor (TCR) .beta.-chain were obtained from
the T-leukemia cell line Jurkat using a single-sided PCR approach based on
5 synthetic oligonucleotides derived from the flanking const.
sequence. Double-stranded cDNA was cleaved by a restriction enzyme
creating cohesive ends, to which an anchor oligonucleotide was
ligated. Since this anchor was complementary to the anti-sense strand of
the known const. region, exclusively the desired ligation product folded
into a stem-loop-structure that was enzymically extended to yield a PCR
template, now flanked at both ends by primer binding sites appropriate for
nested PCR.

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5 synthetic oligonucleotides derived from the flanking const.

sequence. Double-stranded cDNA was cleaved by a restriction enzyme creating cohesive ends, to which an anchor oligonucleotide was ligated. Since this anchor was complementary to the anti-sense strand of the known const. region, exclusively the desired ligation product folded into a stem-loop-structure that was enzymically extended to yield a PCR template, now flanked at both ends by primer binding sites appropriate for nested PCR.

ST RT PCR TCR beta chain cDNA; gene TCRB RTPCR JURKAT cell cDNA

IT TCR (T cell receptors)

RL: BSU (Biological study, unclassified); BIOL (Biological study) (.beta.-chain; complementary anchor PCR of rearranged variable T-cell receptor .beta.-chain cDNA regions)

=> s tcr and rtPCR and oligo and vdj
L6 0 TCR AND RTPCR AND OLIGO AND VDJ

=> s tcr and pcr and vdj
L7 121 TCR AND PCR AND VDJ

=> dup rem 17
PROCESSING COMPLETED FOR L7
L8 48 DUP REM L7 (73 DUPLICATES REMOVED)

=> s 18 and constant
L9 5 L8 AND CONSTANT

=> s 19 1-5 ibib abs kwic
MISSING OPERATOR L9 1-5
The search profile that was entered contains terms or nested terms that are not separated by a logical operator.

=> dis 19 1-5 ibib abs kwic

L9 ANSWER 1 OF 5 MEDLINE
ACCESSION NUMBER: 1999435132 MEDLINE
DOCUMENT NUMBER: 99435132
TITLE: Rearranged T lymphocyte antigen receptor genes as markers of malignant T cells.
AUTHOR: Dreitz M J; Ogilvie G; Sim G K
CORPORATE SOURCE: HESKA Corporation, Ft. Collins, CO 80525, USA.
SOURCE: VETERINARY IMMUNOLOGY AND IMMUNOPATHOLOGY, (1999 Aug 2) 69 (2-4) 113-9.
PUB. COUNTRY: Journal code: XCB. ISSN: 0165-2427. Netherlands
LANGUAGE: English
FILE SEGMENT: Journal; Article; (JOURNAL ARTICLE)
ENTRY MONTH: Priority Journals
ENTRY WEEK: 200001
ENTRY WEEK: 20000104

AB We have recently cloned a number of canine T cell receptor (TCR) Vbeta genes using degenerate oligonucleotides. From the DNA sequences of the resulting clones and the canine Vbeta gene sequences in the literature, seven distinct canine TCR Vbeta genes were identified. Vbeta specific PCR primers were designed for each of the seven TCR Vbeta genes such that under defined conditions, each primer could only amplify a specific TCR Vbeta gene in conjunction with the same 3' constant region (Cbeta) primer. By performing RT-PCR on RNA derived from a source containing T lymphocytes, the presence and expansion of T cells expressing a particular Vbeta gene could be detected. Moreover, the clonality or diversity of a T cell population under analysis could be easily determined by the VDJ junctional sequence of the amplified Vbeta PCR product, in the form of a "DNA fingerprint". These findings have been used to detect canine T cell lymphoma, and could potentially be used to monitor the remission of T cell malignancies in response to treatment.

AB We have recently cloned a number of canine T cell receptor (TCR) Vbeta genes using degenerate oligonucleotides. From the DNA sequences of the resulting clones and the canine Vbeta gene sequences in the literature, seven distinct canine TCR Vbeta genes were identified. Vbeta specific PCR primers were designed for each of the seven TCR Vbeta genes such that under defined conditions, each primer could only amplify a specific TCR Vbeta gene in conjunction with the same 3' constant region (Cbeta) primer. By performing RT-PCR on RNA derived from a source containing T lymphocytes, the presence and expansion of T cells expressing a particular Vbeta . . . be detected. Moreover, the clonality or diversity of a T cell population under analysis could be easily determined by the VDJ junctional sequence of the amplified Vbeta PCR product, in the form of a "DNA fingerprint". These findings have been used to detect canine T cell lymphoma, and. . .

L9 ANSWER 2 OF 5 MEDLINE
ACCESSION NUMBER: 97378032 MEDLINE
DOCUMENT NUMBER: 97378032
TITLE: Enhancer control of local accessibility to V(D)J recombinase.
AUTHOR: McMurtry M T; Hernandez-Munain C; Lauzurica P; Krangel M S
CORPORATE SOURCE: Department of Immunology, Duke University Medical Center, Durham, North Carolina 27710, USA.
CONTRACT NUMBER: GM07071 (NIGMS)
SOURCE: GM41052 (NIGMS) MOLECULAR AND CELLULAR BIOLOGY, (1997 Aug) 17 (8) 4553-61.
PUB. COUNTRY: Journal code: NGY. ISSN: 0270-7306. United States
LANGUAGE: English
FILE SEGMENT: Journal; Article; (JOURNAL ARTICLE)
ENTRY MONTH: Priority Journals
ENTRY WEEK: 199710
ENTRY WEEK: 19971005

AB We have studied the role of transcriptional enhancers in providing recombination signal sequence (RSS) accessibility to V(D)J recombinase by examining mice carrying a transgenic human T-cell receptor (TCR) delta gene minilocus. This transgene is composed of unrearranged variable (Vdelta and Vdelta2), diversity (Ddelta3), joining (Jdelta1 and Jdelta3), and constant (Cdelta) gene segments. Previous data indicated that with the TCR delta enhancer (Edelta) present in the Jdelta3-Cdelta intron, V(D)J recombination proceeds stepwise, first V to D and then VD to J. With the enhancer deleted or mutated, V-to-D rearrangement is intact, but VD-to-J rearrangement is inhibited. We proposed that Edelta is necessary for J segment but not D segment accessibility and that J segment inaccessibility in the enhancerless

minilocus resulted in the observed V(D)J recombination phenotype. In this study, we tested this notion by using ligation-mediated PCR to assess the formation of recombination-activating gene (RAG)-dependent double-strand breaks (DSBs) at RSSs 3' of Ddelta3 and 5' of Jdelta1. In five lines of mice carrying multicopy integrants of constructs that either lacked Edelta or carried an inactivated Edelta, the frequency of DSBs 5' of Jdelta1 was dramatically reduced relative to that in the wild type, whereas the frequency of DSBs 3' of Ddelta3 was unaffected. We interpret these results to indicate that Edelta is required for Jdelta1 but not Ddelta3 accessibility within the minilocus, and we conclude that enhancers regulate V(D)J recombination by providing local accessibility to the recombinase. cis-acting elements other than Edelta must maintain Ddelta3 in an accessible state in the absence of Edelta. The analysis of DSB formation in a single-copy minilocus integrant indicates that efficient DSB formation at the accessible RSS 3' of Ddelta3 requires an accessible partner RSS, arguing that RSS synapsis is required for DSB formation in chromosomal substrates in vivo.

AB . . . enhancers in providing recombination signal sequence (RSS) accessibility to V(D)J recombinase by examining mice carrying a transgenic human T-cell receptor (TCR) delta gene minilocus. This transgene is composed of unrearranged variable (Vdelta and Vdelta2), diversity (Ddelta3), joining (Jdelta1 and Jdelta3), and constant (Cdelta) gene segments. Previous data indicated that with the TCR delta enhancer (Edelta) present in the Jdelta3-Cdelta intron, V(D)J recombination proceeds stepwise, first V to D and then VD to . . . the enhancerless minilocus resulted in the observed V(D)J recombination phenotype. In this study, we tested this notion by using ligation-mediated PCR to assess the formation of recombination-activating gene (RAG)-dependent double-strand breaks (DSBs) at RSSs 3' of Ddelta3 and 5' of Jdelta1. . . .

CN EC 2.7.7.- (DNA Nucleotidyltransferases); EC 2.7.7.- (VDJ recombinase); 0 (Receptors, Antigen, T-Cell, gamma-delta)

L9 ANSWER 3 OF 5 MEDLINE
 ACCESSION NUMBER: 97045028 MEDLINE
 DOCUMENT NUMBER: 97045028
 TITLE: Cloning of T-cell antigen receptor beta chain cDNAs from Atlantic salmon (*Salmo salar*).
 AUTHOR: Hordvik I; Jacob A L J; Charlemagne J; Endresen C
 CORPORATE SOURCE: Department of Fisheries and Marine Biology, High Technology Center University of Bergen, Norway.
 SOURCE: IMMUNOGENETICS, (1996) 45 (1) 9-14.
 PUB. COUNTRY: United States
 LANGUAGE: English
 FILE SEGMENT: Cancer Journals; Priority Journals
 OTHER SOURCE: GENBANK-X97435
 ENTRY MONTH: 199702

AB Atlantic salmon (*Salmo salar*) cDNAs encoding the T-cell antigen receptor beta chain (TCRB) were isolated from leukocyte RNA by reverse transcription - polymerase chain reaction (RT-PCR). Twenty-five distinct cDNA fragments covering the variable (V) - diversity (D) - joining (J) junction and part of the constant (C) region were characterized; the sequences of which indicate interchangeable V/D/J usage and expression in the context of one TCRBC gene. Full-length TCRBC sequence information was derived from a leukocyte cDNA library. Key residues of the salmon TCRBC region are in good agreement with those of other species. One distinct exception is the absence of the hinge region cysteine residue which is involved in covalent bonding between the alpha and beta chain in mammalian TCRs. As in amphibian and avian species, the salmon TCRBC membrane proximal region is considerably shorter than the mammalian. An octamer sequence (GGACAGGG) very similar to amphibian, avian, and mammalian D sequences could be recognized in the VDJ junctions from salmon. The pattern of VDJ variability also indicates that mechanisms like trimming and addition occur in fish as in higher vertebrates. Compared with mammals, a relatively high frequency (32%) of the VDJ junctions in salmon were out of frame.

AB . . . encoding the T-cell antigen receptor beta chain (TCRB) were isolated from leukocyte RNA by reverse transcription - polymerase chain reaction (RT-PCR). Twenty-five distinct cDNA fragments covering the variable (V) - diversity (D) - joining (J) junction and part of the constant (C) region were characterized; the sequences of which indicate interchangeable V/D/J usage and expression in the context of one TCRBC. . . . of the hinge region cysteine residue which is involved in covalent bonding between the alpha and beta chain in mammalian TCRs. As in amphibian and avian species, the salmon TCRBC membrane proximal region is considerably shorter than the mammalian. An octamer sequence (GGACAGGG) very similar to amphibian, avian, and mammalian D sequences could be recognized in the VDJ junctions from salmon. The pattern of VDJ variability also indicates that mechanisms like trimming and addition occur in fish as in higher vertebrates. Compared with mammals, a relatively high frequency (32%) of the VDJ junctions in salmon were out of frame.

L9 ANSWER 4 OF 5 MEDLINE
 ACCESSION NUMBER: 94014793 MEDLINE
 DOCUMENT NUMBER: 94014793
 TITLE: Ex vivo clonotype primer-directed gene amplification to identify malignant T cell repertoires.
 AUTHOR: Beers T; Du T L; Rickert M; Overturf P; Choi Y; Greenberg S J
 CORPORATE SOURCE: Department of Neurology, Roswell Park Cancer Institute, Buffalo, NY 14263.
 SOURCE: JOURNAL OF LEUKOCYTE BIOLOGY, (1993 Oct) 54 (4) 343-50.
 PUB. COUNTRY: United States
 LANGUAGE: English
 FILE SEGMENT: Priority Journals; Cancer Journals
 ENTRY MONTH: 199401

AB A novel strategy that utilizes input genomic DNA and overcomes limitations encountered with traditional RNA reverse transcription-polymerase chain reaction (PCR) amplification methodology is described to screen for T cell receptor (TCR) repertoires. The methodology has been developed to identify individual T cell clonotypes with regard to their unique receptor beta chain variable/diversity/joining (VDJ) region gene rearrangement. The technique avoids preselection for a given antigen specificity and is therefore independent of artificial bias introduced by in vitro cell population expansion. This technique was used to detect and identify genetically of malignant clones from heterogeneous mononuclear cell populations from an array of hemato-oncological

disorders, including mycosis fungoides/Sezary Syndrome, adult T cell leukemia, and large granular lymphoproliferative disease. An initial primary PCR, directed by a TCR-J beta generic primer and a complement of family-specific TCR-V beta primers, defines predominant T cell receptor variable gene usage. Use of a TCR-J beta generic primer supplants the use of a constant region primer anchor and thus eliminates the need to target mRNA. The process of variable gene screening also expedites gene sequencing. By sequencing through the VDJ juxtaposed region, i.e., the third complementarity determinant region, clonotype-specific primers are developed and used in a secondary clonotype primer-directed PCR (CPD-PCR) to detect, with extreme sensitivity and specificity, unique T cell clonal repertoires. Analysis of the products of the CPD-PCR permits the detection of a single malignant cell among one million polyclonal cells and supercedes the constraints of prior studies that provide a limited evaluation of family variable gene repertoire usage. This strategy may be applied in the detection of minimal residual disease, in surveillance after induction of disease-free states, and in analyzing the effectiveness of purging autologous bone marrow of malignant clones.

AB A novel strategy that utilizes input genomic DNA and overcomes limitations encountered with traditional RNA reverse transcription-polymerase chain reaction (PCR) amplification methodology is described to screen for T cell receptor (TCR) repertoires. The methodology has been developed to identify individual T cell clonotypes with regard to their unique receptor beta chain variable/diversity/joining (VDJ) region gene rearrangement. The technique avoids preselection for a given antigen specificity and is therefore independent of artificial bias introduced. . . . array of hemato-oncological disorders, including mycosis fungoides/Sezary Syndrome, adult T cell leukemia, and large granular lymphoproliferative disease. An initial primary PCR, directed by a TCR-J beta generic primer and a complement of family-specific TCR-V beta primers, defines predominant T cell receptor variable gene usage. Use of a TCR-J beta generic primer supplants the use of a constant region primer anchor and thus eliminates the need to target mRNA. The process of variable gene screening also expedites gene sequencing. By sequencing through the VDJ juxtaposed region, i.e., the third complementarity determinant region, clonotype-specific primers are developed and used in a secondary clonotype primer-directed PCR (CPD-PCR) to detect, with extreme sensitivity and specificity, unique T cell clonal repertoires. Analysis of the products of the CPD-PCR permits the detection of a single malignant cell among one million polyclonal cells and supercedes the constraints of prior studies. . . .

L9 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:98766 CAPLUS

DOCUMENT NUMBER: 132:165134

TITLE: Canine T cell receptor .beta.-chain variable regions and their nucleic acids

INVENTOR(S): Dreitz, Matthew J.; Sim, Gek-Kee

PATENT ASSIGNEE(S): Heska Corporation, USA

SOURCE: PCT Int. Appl., 161 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000006732	A2	20000210	WO 1999-US17284	19990730
WO 2000006732	A3	20000504		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9952444	A1	20000221	AU 1999-52444	19990730
WO 2001007616	A1	20010201	WO 2000-US6742	20000310

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:
US 1998-94930 19980731
US 1999-359084 19990722
WO 1999-US17284 19990730
US 1999-447399 19991123

AB The present invention provides for isolated T cell receptor .beta.-chain variable region (TCRV.beta.) proteins, isolated TCR V.beta. nucleic acid mols., antibodies directed against TCR V.beta. proteins, and compds. derived therefrom that regulate the immune response of an animal. Seven different V.beta. isoforms from Canis familiaris and their cDNA sequences are provided. The sequences are useful for detection of expansion of T cells and for the diagnosis and treatment of TCR-assocd. diseases.

AB The present invention provides for isolated T cell receptor .beta.-chain variable region (TCRV.beta.) proteins, isolated TCR V.beta. nucleic acid mols., antibodies directed against TCR V.beta. proteins, and compds. derived therefrom that regulate the immune response of an animal. Seven different V.beta. isoforms from Canis familiaris and their cDNA sequences are provided. The sequences are useful for detection of expansion of T cells and for the diagnosis and treatment of TCR-assocd. diseases.

ST TCR receptor beta chain cDNA sequence dog

IT Allergy inhibitors
Anti-infective agents
Antiasthmatics
Antibacterial agents
Antidiabetic agents
Antirheumatic agents
Antitumor agents
Antiviral agents
Dog (Canis familiaris)
PCR (polymerase chain reaction)
Parasiticides

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Vaccines
(canine T cell receptor .beta.-chain variable regions and their nucleic
acids)
IT TCR (T cell receptors)
RL: ARG (Analytical reagent use); BOC (Biological occurrence); PRP
(Properties); THU (Therapeutic use); ANST (Analytical study); BIOL
(Biological study); OCCU (Occurrence); USES (Uses)
(canine T cell receptor .beta.-chain variable regions and their nucleic
acids)
IT cDNA sequences
(for canine T cell receptor .beta.-chain VDJ regions)
IT Protein sequences
(of canine T cell receptor .beta.-chain VDJ regions)
IT 258323-08-9 258323-09-0 258323-10-3 258323-11-4 258323-12-5
258323-13-6 258323-14-7 258323-15-8 258323-16-9 258325-19-8
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical
study); BIOL (Biological study); USES (Uses)
(primer for const. region; canine T cell receptor
.beta.-chain variable regions and their nucleic acids)

=> dis his

(FILE 'HOME' ENTERED AT 10:44:33 ON 18 APR 2001)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 10:44:42 ON 18 APR 2001
L1 0 S MJ? AND TCR AND (RTPCR OR PCR)
L2 0 S MJ? AND APLPA
L3 6 S MJ? AND TCR
L4 3 DUP REM L3 (3 DUPLICATES REMOVED)
L5 1 S TCR AND RTPCR AND OLIGO?
L6 0 S TCR AND RTPCR AND OLIGO AND VDJ
L7 121 S TCR AND PCR AND VDJ
L8 48 DUP REM L7 (73 DUPLICATES REMOVED)
L9 5 S L8 AND CONSTANT

=> s ((primer? (5N) (Valpha or Vbeta)) and TCR
UNMATCHED LEFT PARENTHESIS '({PRIMER?'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s ((primer? (5N) (Valpha or Vbeta))) and TCR
L10 17 ((PRIMER? (5N) (VALPHA OR VBETA))) AND TCR

=> dup rem l10
PROCESSING COMPLETED FOR L10
L11 12 DUP REM L10 (5 DUPLICATES REMOVED)

=> dis l11 1-12 kwic

L11 ANSWER 1 OF 12 MEDLINE
AB The T-cell receptor (TCR) CDR3 length heterogeneity is formed
during recombination of individual Vbeta gene families. We hypothesized
that CDR3 length diversity could be used to assess the fundamental
differences within the TCR repertoire of CD45RA and CD45RO
T-cell subpopulations. By using PCR-based spectratyping, nested
primers for all 24 human Vbeta families were developed
to amplify CDR3 lengths in immunomagnetically selected CD45RA and CD45RO
subsets within both CD4(+) and CD8(+) T-cell. . . . of the CDR3 length
diversity within CD45RA and CD45RO T cells provides a more accurate
measure of disturbances in the TCR repertoire than analysis of
unfractionated CD4 and CD8 T cells.

L11 ANSWER 2 OF 12 MEDLINE
AB . . . . in the peripheral blood, liver, and spleen of Patient 2. In the
two patients, T-cell receptor-beta and alpha-chain variable region (
TCR Vbeta and V alpha) repertoires in peripheral mononuclear cells
were analyzed at the time of disease onset and at disease. . . . of a
specific Vbeta family member was observed, a clonal analysis was performed
by PCR using beta-chain joining region (Jbeta) primers. The
clonality of specific Vbeta-Jbeta fragments was confirmed by a
single strand confirmation polymorphism (SSCP) analysis. RESULTS: Although
there was no preferential usage of Vbeta. . . .

L11 ANSWER 3 OF 12 BIOSIS COPYRIGHT 2001 BIOSIS
AB The examination of T-cell receptor (TCR) repertoires has an
important role in the study of lymphoproliferative disorders and
autoimmune diseases. Analysis of the complementarity-determining region 3
(CDR3) of the TCR beta chain is used to assess the clonality of
T-cell populations. We developed a rapid fluorescence-based method for
CDR3 length analysis of expressed TCR gene families. TCR
beta chain complementary DNA is amplified by a nested polymerase chain
reaction with Vbeta family-specific oligonucleotide
primers and a fluorochrome-labeled Cbeta primer. The polymerase
chain reaction products were analyzed on a compact automated DNA
sequencing system (OpenGene. . . .

L11 ANSWER 4 OF 12 BIOSIS COPYRIGHT 2001 BIOSIS
AB . . . T-cell trigger and is determined by a T-cell driven immune response,
and to assess the clonality of CD4+ and CD8+ Tcr usage in
subjects with FASSC. Materials and methods We used reverse transcription
polymerase chain reaction with specific Valpha- and
Vbeta-chain primers to identify the Tcr gene
usage in biopsy material, bronchoalveolar lavage fluid or peripheral blood
from our subjects. Results We found individual-specific restriction of. . .
between lung and peripheral blood lymphocyte Vbeta-families in CD8+
T-cells (P = 0.0007). Conclusion We conclude that there is individual
Tcr Valpha- and Vbeta-expression bias in subjects with fibrosing
alveolitis.

L11 ANSWER 5 OF 12 MEDLINE
AB We have recently cloned a number of canine T cell receptor (TCR)
Vbeta genes using degenerate oligonucleotides. From the DNA sequences of
the resulting clones and the canine Vbeta gene sequences in the
literature, seven distinct canine TCR Vbeta genes were
identified. Vbeta specific PCR primers were designed
for each of the seven TCR Vbeta genes such that under defined
conditions, each primer could only amplify a specific TCR Vbeta
gene in conjunction with the same 3' constant region (Cbeta) primer. By
performing RT-PCR on RNA derived from a. . . .

L11 ANSWER 6 OF 12 MEDLINE
AB . . . lines previously established with interleukin-2 (IL-2) and IL-7

```

from the skin and from the blood. Analysis of the T-cell receptor (TCR) Vbeta gene expression showed that the tumor cells, which were shown to have a trisomy 7 by fluorescent in situ. . . . monoclonal antibodies indicated that only Vbeta13 could be detected on the cell membrane of the tumor cells. Analysis of the TCR Vbeta gene expression of the clones showed that TC5 and TC7 expressed a unique TCR-Vbeta transcript, corresponding, respectively, to Vbeta5/Jbeta2.3 and Vbeta17/Jbeta2.7 gene segments. To determine whether these reactive T lymphocytes were present in vivo, we used specific primers corresponding to TC5- and TC7-Vbeta TCR transcripts. The results showed that both cytotoxic T-cell clones were present at the lesional skin site and amplified in vitro. . . .

L11 ANSWER 7 OF 12 MEDLINE
TI TCR-Vbeta usage in the thymus and blood of myasthenia gravis patients. . . . DUPLICATE 4

AB to whether sAg play a role in the pathogenesis of MG. We investigated the frequency of use of the different TCR Vbeta families by the thymus and blood T cells in MG patients and in control subjects, using a multi-primer PCR assay. Identical TCR-Vbeta usage was found in the thymus of MG patients and controls, except Vbeta2, which showed a small increase in MG. . . . the immunodominance of certain AChR epitopes, or the action of a sAg outside the thymus. The minimal differences in the TCR-Vbeta usage in the blood and thymus of control subjects might be due to expansion of T cell clones specific for. . . .

L11 ANSWER 8 OF 12 MEDLINE

AB clinical application of such analyses has been limited. Here we have established novel primers to anneal with T cell receptor (TCR) beta genes of multiple Vbeta families and applied them to reverse transcription-polymerase chain reaction-single strand conformation polymorphism (RT-PCR-SSCP) analysis to evaluate peripheral T cell clonality of autoimmune disease patients. As a result, the new Vbeta primers could detect accumulating T cell clones in the periphery of healthy individuals and patients. It was revealed that patients with. . . . number of clonal accumulations of peripheral T cells compared with normal individuals. Thus, the RT-PCR-SSCP system using the new multifamily Vbeta primers is the first such laboratory examination to detect T cell clonal expansion, and will provide a simple and sensitive tool. . . .

L11 ANSWER 9 OF 12 MEDLINE

AB patients with toxic liver injury were extracted and analysed using a semiquantitative RT-PCR with a panel of T cell receptor Vbeta family specific primers. After agarose gel electrophoresis, the distribution of T cell receptor (TCR) Vbeta molecules was assessed by densitometry. Furthermore, results were compared to the TCR Vbeta distribution of 10 healthy blood donors. RESULTS: Four of 12 patients with untreated autoimmune hepatitis but no patients with chronic hepatitis C and toxic liver injury showed a significant overexpression of TCR Vbeta3 (17.8% +/- 2.6% vs. 9.3% +/- 4.6%; p = 0.01) and three an overexpression of Vbeta13.1 (14.6% +/- 2.3% vs. 6.6% +/- 3.5%; p = 0.02) molecules compared to the TCR Vbeta-distribution in healthy blood donors. In addition, Vbeta3+ T cells were found enriched in the liver tissue compared to autologous. . . . in the liver tissue from one of three patients with overexpression. CONCLUSIONS: In autoimmune hepatitis a disease specific compartmentalisation of TCR Vbeta3+ T cells was observed in the liver tissues. Although their specificity was unknown, this might indicate that these infiltrating. . . . DUPLICATE 5

L11 ANSWER 10 OF 12 MEDLINE

TI TCR vbeta usage of TSH receptor-specific CD4+ T cells in Graves' disease patients and healthy humans. . . .
AB have CD4+ T cells specific for self-components. Since autoreactive T cells in autoimmune patients may use a limited number of TCR V-region genes, we investigated here whether this also occurs for the potentially autoreactive CD4+ cells present in healthy persons. We. . . . repertoire had been characterized previously: each line recognized one or a few TSHr peptides, different for each subject. We determined their TCR Vbeta usage by a semi-quantitative reverse transcriptase PCR assay, using primers specific for each known human Vbeta region family, in conjunction with a constant region primer. Six lines preferentially used one Vbeta family (42-94%), different for each line. In all lines, three or less Vbeta families accounted for approximately 60% or more. . . . CD4+ cells involved in autoimmune diseases are likely recruited from that pool, since they have similar characteristics of epitope and TCR repertoire as the CD4+ cells specific for the same autoantigen in healthy subjects. Copyright 1997 Academic Press Limited.

L11 ANSWER 11 OF 12 MEDLINE

AB was employed to examine T cells in middle ear effusions in patients with OME for utilization of T cell receptor (TCR) variable region genes. Specimens of RNA were extracted from 13 ears of 12 patients (9 children and 3 adults). Oligonucleotide primers specific for individual TCR Vbeta gene families were used to amplify TCR gene products in each sample. Although the number of Vbeta families utilized by each sample varied from 1 family to. . . .

L11 ANSWER 12 OF 12 MEDLINE

AB We analyzed the T-cell repertoire in patients transplanted with bone marrow from an HLA identical sibling by determining the TCR diversity through Vbeta-CDR3-size spectratyping with Vbeta /Cbeta- and Vbeta/Jbeta-specific primers. Using the Vbeta/Cbeta primers, we observed limited TCR diversity only in recipients of a T-cell-depleted graft, whereas the TCR diversity of patients transplanted with an unmanipulated graft seemed to be indistinguishable from the one of a normal individual. However, with Vbeta/Jbeta-specific primers, increase of the resolution by approximately 10-fold also allowed the detection of imbalances in the TCR repertoire of recipients of an unmanipulated graft. This demonstrates that when high numbers of T cells are cotransfused with marrow, the TCR repertoire is more complete but still not as complete as in normal individuals, thereby emphasizing the important role of coinfection. . . .

=> dis l11 1-12 ibib abs

L11 ANSWER 1 OF 12 MEDLINE

ACCESSION NUMBER: 2001136996 MEDLINE
 DOCUMENT NUMBER: 20517578
 TITLE: T-Cell receptor Vbeta repertoire CDR3 length diversity differs within CD45RA and CD45RO T-cell subsets in healthy and human immunodeficiency virus-infected children.
 AUTHOR: Kou Z C; Puhf J S; Rojas M; McCormack W T; Goodenow M M; Sleasman J W
 CORPORATE SOURCE: Department of Pediatrics, Division of Immunology and Infectious Diseases, University of Florida College of Medicine, Gainesville, Florida 32610-0296, USA.
 CONTRACT NUMBER: R01 HD32259 (NICHD)
 R01 HL58005 (NHLBI)
 RR0082 (NCRR)
 SOURCE: CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY, (2000 Nov) 7 (6) 953-9.
 Journal code: CB7. ISSN: 1071-412X.
 PUB. COUNTRY: United States
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200103

AB The T-cell receptor (TCR) CDR3 length heterogeneity is formed during recombination of individual Vbeta gene families. We hypothesized that CDR3 length diversity could be used to assess the fundamental differences within the TCR repertoire of CD45RA and CD45RO T-cell subpopulations. By using PCR-based spectratyping, nested primers for all 24 human Vbeta families were developed to amplify CDR3 lengths in immunomagnetically selected CD45RA and CD45RO subsets within both CD4(+) and CD8(+) T-cell populations. Umbilical cord blood mononuclear cells or peripheral blood mononuclear cells obtained from healthy newborns, infants, and children, as well as human immunodeficiency virus (HIV)-infected children, were analyzed. All T-cell subsets from newborn and healthy children demonstrated a Gaussian distribution of CDR3 lengths in separated T-cell subsets. In contrast, HIV-infected children had a high proportion of predominant CDR3 lengths within both CD45RA and CD45RO T-cell subpopulations, most commonly in CD8(+) CD45RO T cells. Sharp differences in clonal dominance and size distributions were observed when cells were separated into CD45RA or CD45RO subpopulations. These differences were not apparent in unfractionated CD4(+) or CD8(+) T cells from HIV-infected subjects. Sequence analysis of predominant CDR3 lengths revealed oligoclonal expansion within individual Vbeta families. Analysis of the CDR3 length diversity within CD45RA and CD45RO T cells provides a more accurate measure of disturbances in the TCR repertoire than analysis of unfractionated CD4 and CD8 T cells.

L11 ANSWER 2 OF 12 MEDLINE DUPLICATE 1

ACCESSION NUMBER: 1999208300 MEDLINE
 DOCUMENT NUMBER: 99208300
 TITLE: Clonal change of infiltrating T-cells in children with familial hemophagocytic lymphohistiocytosis: possible association with Epstein-Barr virus infection.
 AUTHOR: Ishii E; Kimura N; Kato K; Sako M; Nagano M; Nakagawa A; Okamura T; Yamaguchi H; Kawa K; Hara T
 CORPORATE SOURCE: Division of Pediatrics, Hamanomachi Hospital, Fukuoka, Japan.
 SOURCE: CANCER, (1999 Apr 1) 85 (7) 1636-43.
 Journal code: CL2. ISSN: 0008-543X.
 PUB. COUNTRY: United States
 LANGUAGE: English
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
 ENTRY MONTH: 199907
 ENTRY WEEK: 19990702

AB BACKGROUND: Although familial hemophagocytic lymphohistiocytosis (FHL) has been considered a T-cell disorder, to the authors' knowledge there are no previous reports on the clonal basis of FHL. In the current study the authors analyzed the clonality of T-cells in two FHL patients at the time of disease onset and at disease progression. METHODS: Patient 1 had FHL and died of recurrent disease 4 months after bone marrow transplantation (BMT). His liver and spleen showed massive infiltrations of CD3+, CD4-, and CD8+ T-cells. The Epstein-Barr virus (EBV) genome was detected by in situ hybridization. Patient 2 also had FHL and died of progressive disease 9 weeks after the onset of disease despite chemotherapy. A polymerase chain reaction (PCR) analysis showed positive EBV genome in the peripheral blood, liver, and spleen of Patient 2. In the two patients, T-cell receptor-beta and alpha-chain variable region (TCR Vbeta and V alpha) repertoires in peripheral mononuclear cells were analyzed at the time of disease onset and at disease progression by the inverse PCR method. When a high usage (> 15%) of a specific Vbeta family member was observed, a clonal analysis was performed by PCR using beta-chain joining region (Jbeta) primers. The clonality of specific Vbeta-Jbeta fragments was confirmed by a single strand confirmation polymorphism (SSCP) analysis. RESULTS: Although there was no preferential usage of Vbeta in Patient 1, the exclusive expression of Jbeta1.2 for Vbeta13 was observed. A high frequency of Vbeta13 also was observed at the time of disease progression, but the Jbeta fragment for Vbeta13 was polyclonal. In Patient 2, the restricted usage of Jbeta1.6 for Vbeta5a was observed at the time of disease onset, whereas Jbeta1.1 and 1.2 for Vbeta4 were observed exclusively at the time of disease progression. The clonality of Vbeta13-Jbeta1.2 in Patient 1 and Vbeta5a-Jbeta1.6 and Vbeta4-Jbeta1.1/Jbeta1.2 in Patient 2 was confirmed by SSCP analysis. CONCLUSIONS: These findings suggest that the polyclonal T-cell lymphoproliferative disease associated with EBV was induced after BMT in Patient 1, and that the clonal change of expanded T-cells also was induced by EBV in Patient 2. The clonal analysis of T-cells is a useful tool to clarify the pathogenesis of FHL.

L11 ANSWER 3 OF 12 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1999:256318 BIOSIS
 DOCUMENT NUMBER: PREV199900256318
 TITLE: An automated method for the analysis of T-cell receptor repertoires: Rapid RT-PCR fragment length analysis of the T-cell receptor beta chain complementarity-determining region 3.
 AUTHOR(S): Lue, Cummins (1); Mitani, Yuichi; Crew, Mark D.; George, James F.; Fink, Louis M.; Schichman, Steven A.
 CORPORATE SOURCE: (1) Department of Medicine, University of Arkansas for Medical Sciences, 4301 West Markham, Slot 509, Little Rock, AR, 72205 USA
 SOURCE: American Journal of Clinical Pathology, (May, 1999) Vol. 111, No. 5, pp. 683-690.

ISSN: 0002-9173.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The examination of T-cell receptor (TCR) repertoires has an important role in the study of lymphoproliferative disorders and autoimmune diseases. Analysis of the complementarity-determining region 3 (CDR3) of the TCR beta chain is used to assess the clonality of T-cell populations. We developed a rapid fluorescence-based method for CDR3 length analysis of expressed TCR gene families. TCR beta chain complementary DNA is amplified by a nested polymerase chain reaction with Vbeta family-specific oligonucleotide primers and a fluorochrome-labeled Cbeta primer. The polymerase chain reaction products were analyzed on a compact automated DNA sequencing system (OpenGene system, Visible Genetics, Toronto, Ontario). To demonstrate the usefulness of our technique, we examined the CDR3 length distribution of peripheral blood T cells from a healthy subject, intestinal T cells from a patient with ulcerative colitis, and the T-cell leukemia cell line Jurkat. The analysis revealed polyclonal, oligoclonal, and monoclonal CDR3 distributions, respectively, for the 3 T-cell populations. Our new method shows virtually identical CDR3 length patterns compared with the traditional radioisotope-based method. The new technique offers the convenience of rapid throughput, nonradioactive labeling, and quality data analysis.

L11 ANSWER 4 OF 12 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1999:195044 BIOSIS

DOCUMENT NUMBER: PREV199900195044

TITLE: T-cell receptor gene usage in patients with fibrosing alveolitis and control subjects.

AUTHOR(S): Lympny, P. A.; Southcott, A. M.; Welsh, K. I.; Black, C. M.; Boylston, A. W.; du Bois, R. M. (1)

CORPORATE SOURCE: (1) Interstitial Lung Disease Unit, Department of Occupational and Environmental Medicine, Imperial College of Science, Technology and Medicine, 18 Manresa Road, Emmanuel Kaye Building, London, SW3 6LR UK

SOURCE: European Journal of Clinical Investigation, (Feb., 1999) Vol. 29, No. 2, pp. 173-181.
ISSN: 0014-2972.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Background Fibrosing alveolitis is characterized by inflammation, fibrosis and increased numbers of activated CD4+ T-cells in the lower respiratory tract. The aims of this study were to compare the T-cell antigen receptor repertoire in the lungs of subjects with fibrosing alveolitis systemic sclerosis (FASSc) with cryptogenic fibrosing alveolitis (CFA) and normal control subjects, to determine whether FASSc is driven by a specific T-cell trigger and is determined by a T-cell driven immune response, and to assess the clonality of CD4+ and CD8+ TcR usage in subjects with FASSc. Materials and methods We used reverse transcription polymerase chain reaction with specific Valpha- and Vbeta-chain primers to identify the TcR gene usage in biopsy material, bronchoalveolar lavage fluid or peripheral blood from our subjects. Results We found individual-specific restriction of Valpha- and Vbeta-chain usage in lung biopsies from patients and control subjects. To establish whether this was due to expression bias in the CD4+ or CD8+ T-cells and was restricted to the lung, the alphabeta-T-cell receptor chain usage was assessed in T-cell subsets separated from the lungs of patients with fibrosing alveolitis and was compared with that of the peripheral blood. There was no consistent difference in the expression of any variable family chain among the population studied, although there was a significant difference between lung and peripheral blood lymphocyte Vbeta-families in CD8+ T-cells (P = 0.0007). Conclusion We conclude that there is individual TcR Valpha- and Vbeta-expression bias in subjects with fibrosing alveolitis.

L11 ANSWER 5 OF 12 MEDLINE

DUPLICATE 2

ACCESSION NUMBER: 1999435132 MEDLINE

DOCUMENT NUMBER: 99435132

TITLE: Rearranged T lymphocyte antigen receptor genes as markers of malignant T cells.

AUTHOR: Dreitz M J; Ogilvie G; Sim G K

CORPORATE SOURCE: HESKA Corporation, Ft. Collins, CO 80525, USA.

SOURCE: VETERINARY IMMUNOLOGY AND IMMUNOPATHOLOGY, (1999 Aug 2) 69 (2-4) 113-9.

Journal code: XCB. ISSN: 0165-2427.

PUB. COUNTRY: Netherlands

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200001

ENTRY WEEK: 20000104

AB We have recently cloned a number of canine T cell receptor (TCR) Vbeta genes using degenerate oligonucleotides. From the DNA sequences of the resulting clones and the canine Vbeta gene sequences in the literature, seven distinct canine TCR Vbeta genes were identified. Vbeta specific PCR primers were designed for each of the seven TCR Vbeta genes such that under defined conditions, each primer could only amplify a specific TCR Vbeta gene in conjunction with the same 3' constant region (Cbeta) primer. By performing RT-PCR on RNA derived from a source containing T lymphocytes, the presence and expansion of T cells expressing a particular Vbeta gene could be detected. Moreover, the clonality or diversity of a T cell population under analysis could be easily determined by the VDJ junctional sequence of the amplified Vbeta PCR product, in the form of a "DNA fingerprint". These findings have been used to detect canine T cell lymphoma, and could potentially be used to monitor the remission of T cell malignancies in response to treatment.

L11 ANSWER 6 OF 12 MEDLINE

DUPLICATE 3

ACCESSION NUMBER: 1998261461 MEDLINE

DOCUMENT NUMBER: 98261461

TITLE: Isolation of tumor-specific cytotoxic CD4+ and CD4+CD8dim+ T-cell clones infiltrating a cutaneous T-cell lymphoma.

AUTHOR: Bagot M; Echchakir H; Mami-Chouaib F; Delfau-Larue M H;

Charue D; Bernheim A; Chouaib S; Boumsell L; Bensussan A

CORPORATE SOURCE: INSERM U448, Paris XII University, Paris, France.

SOURCE: BLOOD, (1998 Jun 1) 91 (11) 4331-41.

Journal code: A8G. ISSN: 0006-4971.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer

Journals
ENTRY MONTH: 199809
ENTRY WEEK: 19980901

AB We have isolated several T-cell clones from lymphocytes infiltrating a human major histocompatibility class (MHC) II negative cutaneous T-cell lymphoma (CTCL). We describe here two of these clones, TC5 and TC7, with, respectively, a CD4(+)CD8dim+ and CD4(+)CD8(-) phenotype. Both clones mediated a specific MHC class I-restricted cytotoxic activity toward the fresh autologous tumor cells, and autologous tumor cell lines previously established with interleukin-2 (IL-2) and IL-7 from the skin and from the blood. Analysis of the T-cell receptor (TCR) Vbeta gene expression showed that the tumor cells, which were shown to have a trisomy 7 by fluorescent in situ hybridization, expressed Vbeta7/Jbeta2.3, Vbeta13/Jbeta2.5, and Vbeta22/Jbeta2.5 rearrangements. Phenotypic analysis using specific anti-Vbeta monoclonal antibodies indicated that only Vbeta13 could be detected on the cell membrane of the tumor cells. Analysis of the TCR Vbeta gene expression of the clones showed that TC5 and TC7 expressed a unique TCR-Vbeta transcript, corresponding, respectively, to Vbeta5/Jbeta2.3 and Vbeta17/Jbeta2.7 gene segments. To determine whether these reactive T lymphocytes were present in vivo, we used specific primers corresponding to TC5- and TC7-Vbeta TCR transcripts. The results showed that both cytotoxic T-cell clones were present at the lesional skin site and amplified in vitro. TC7 was found in the patient peripheral blood invaded by tumoral cells, whereas TC5 was not, indicating that the repertoire of the reactional lymphocytes differs in the blood and at the tumor site. These results show for the first time the presence of reactive T lymphocytes with CD4 or double-positive phenotype infiltrating a CTCL. These findings raise the question of the role of these antitumoral effector T cells in the tumor growth.

L11 ANSWER 7 OF 12 MEDLINE
ACCESSION NUMBER: 1999096524 MEDLINE
DOCUMENT NUMBER: 99096524
TITLE: TCR-Vbeta usage in the thymus and blood of myasthenia gravis patients.
AUTHOR: Navaneetham D; Penn A S; Howard JF Jr; Conti-Fine B M
CORPORATE SOURCE: College of Biological Sciences, University of Minnesota, St. Paul, MN, 55108, USA.
CONTRACT NUMBER: NS 23919 (NINDS)
SOURCE: NS 17904 (NINDS)
JOURNAL OF AUTOIMMUNITY, (1998 Dec) 11 (6) 621-33.
PUB. COUNTRY: Journal code: ADL. ISSN: 0896-8411.
ENGLAND: United Kingdom
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY WEEK: 19990402
DUPLICATE 4

AB In myasthenia gravis (MG) the muscle acetylcholine receptor (AChR) is the target of an autoimmune response. The anti-AChR response may originate in the thymus, which is abnormal in most MG patients and contains anti-AChR T and B cells. Microbial superantigens (sAg) may trigger autoimmune responses and in this study we sought clues as to whether sAg play a role in the pathogenesis of MG. We investigated the frequency of use of the different TCR Vbeta families by the thymus and blood T cells in MG patients and in control subjects, using a multi-primer PCR assay. Identical TCR-Vbeta usage was found in the thymus of MG patients and controls, except Vbeta2, which showed a small increase in MG patients' thymus. Blood T cells of MG patients used Vbeta4, Vbeta6, Vbeta15, Vbeta16 and Vbeta24 significantly more than those of the controls. Vbeta4 and Vbeta6 are the gene families most frequently used by anti-AChR CD4(+) cells in MG patients. Blood T cells from MG patients used Vbeta12, Vbeta14, Vbeta17 and Vbeta18 significantly less than controls. MG patients used Vbeta4 and Vbeta6 significantly more in the blood than in the thymus, while the opposite occurred for Vbeta7, Vbeta12 and Vbeta14. Controls used Vbeta17 more and Vbeta24 less in the blood than in the thymus. The preferential expansion of Vbeta4 and Vbeta6 in MG patients might reflect the immunodominance of certain AChR epitopes, or the action of a sAg outside the thymus. The minimal differences in the TCR-Vbeta usage in the blood and thymus of control subjects might be due to expansion of T cell clones specific for common antigens. Identical Vbeta usage in the thymus of MG patients and controls does not support an important role of the thymus as the location of anti-AChR sensitization when MG is clinically evident. The differences observed in the Vbeta usage in blood and thymus of MG patients are likely to be due to preferential Vbeta usage by the anti-AChR T cells in the blood. Copyright 1998 Academic Press

L11 ANSWER 8 OF 12 MEDLINE
ACCESSION NUMBER: 1998252377 MEDLINE
DOCUMENT NUMBER: 98252377
TITLE: Frequent clonal expansion of peripheral T cells in patients with autoimmune diseases: a novel detecting system possibly applicable to laboratory examination.
AUTHOR: Masuko-Hongo K; Kato T; Suzuki S; Sekine T; Kurokawa M; Ueda S; Yamada A; Nishioka K; Yamamoto K
CORPORATE SOURCE: Rheumatology, Immunology and Genetics Program, Institute of Medical Sciences, St. Marianna University, Kanagawa, Japan.. GBH01723@niftyserve.or.jp
SOURCE: JOURNAL OF CLINICAL LABORATORY ANALYSIS, (1998) 12 (3) 162-7.
PUB. COUNTRY: Journal code: JLA. ISSN: 0887-8013.
United States
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY WEEK: 19980901

AB To investigate T cell involvement in antigen-specific immune responses, it is important to detect accumulating T cells at a clonal level in vivo. However, thus far the clinical application of such analyses has been limited. Here we have established novel primers to anneal with T cell receptor (TCR) beta genes of multiple Vbeta families and applied them to reverse transcription-polymerase chain reaction-single strand conformation polymorphism (RT-PCR-SSCP) analysis to evaluate peripheral T cell clonality of autoimmune disease patients. As a result, the new Vbeta primers could detect accumulating T cell clones in the periphery of healthy individuals and patients. It was revealed that patients with autoimmune diseases such as systemic lupus erythematosus (SLE) had a larger number of clonal accumulations of peripheral T cells compared with normal individuals. Thus, the RT-PCR-SSCP system using the new multifamily Vbeta primers is the first such

laboratory examination to detect T cell clonal expansion, and will provide a simple and sensitive tool to aid in the diagnosis and also in the investigation of the pathogenesis of autoimmune diseases.

L11 ANSWER 9 OF 12 MEDLINE
ACCESSION NUMBER: 1998140913 MEDLINE
DOCUMENT NUMBER: 98140913
TITLE: Limited T cell receptor Vbeta-chain repertoire of liver-infiltrating T cells in autoimmune hepatitis.
AUTHOR: Arenz M; Meyer zum Buschenfelde K H; Lohr H F
CORPORATE SOURCE: Ist. Dept. of Internal Medicine, Johannes Gutenberg-University, Mainz, Germany.
SOURCE: JOURNAL OF HEPATOLOGY, (1998 Jan) 28 (1) 70-7.
PUB. COUNTRY: Journal code: IBS. ISSN: 0168-8278.
PUB. COUNTRY: Denmark
LANGUAGE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: English
ENTRY MONTH: Priority Journals
ENTRY WEEK: 199806
ENTRY WEEK: 19980602
AB BACKGROUND/AIMS: To characterize the cellular immune reactions in autoimmune hepatitis, the T cell receptor repertoire of liver-infiltrating and circulating T cells was studied. METHODS: Nucleic acids of liver-tissue and peripheral blood-derived T cells from 12 patients with untreated autoimmune hepatitis, four patients with chronic hepatitis C and three patients with toxic liver injury were extracted and analysed using a semiquantitative RT-PCR with a panel of T cell receptor Vbeta family specific primers. After agarose gel electrophoresis, the distribution of T cell receptor (TCR) Vbeta molecules was assessed by densitometry. Furthermore, results were compared to the TCR Vbeta distribution of 10 healthy blood donors. RESULTS: Four of 12 patients with untreated autoimmune hepatitis but no patients with chronic hepatitis C and toxic liver injury showed a significant overexpression of TCR Vbeta3 (17.8% +/- 2.6% vs. 9.3% +/- 4.6%; p = 0.01) and three an overexpression of Vbeta13.1 (14.6% +/- 2.3% vs. 6.6% +/- 3.5%; p = 0.02) molecules compared to the TCR Vbeta-distribution in healthy blood donors. In addition, Vbeta3+ T cells were found enriched in the liver tissue compared to autologous peripheral blood in three autoimmune hepatitis patients (15.3% +/- 7.0% vs. 5.2% +/- 3.1%; L/B ratio: 2.9), while Vbeta13.1+ T cells were enriched in the liver tissue from one of three patients with overexpression. CONCLUSIONS: In autoimmune hepatitis a disease specific compartmentalisation of TCR Vbeta3+ T cells was observed in the liver tissues. Although their specificity was unknown, this might indicate that these infiltrating T cells could have relevance for abnormal immunoregulation.

L11 ANSWER 10 OF 12 MEDLINE
ACCESSION NUMBER: 1998018742 MEDLINE
DOCUMENT NUMBER: 98018742
TITLE: TCR vbeta usage of TSH receptor-specific CD4+ T cells in Graves' disease patients and healthy humans.
AUTHOR: Raju R; Navaneetham D; Kellermann S A; Freeman S L; Morris J C; McCormick D J; Conti-Fine B M
CORPORATE SOURCE: Department of Biochemistry, University of Minnesota, St Paul, MN 55108, USA.
CONTRACT NUMBER: NS 23919 (NINDS)
SOURCE: JOURNAL OF AUTOIMMUNITY, (1997 Oct) 10 (5) 479-89.
PUB. COUNTRY: Journal code: ADL. ISSN: 0896-8411.
PUB. COUNTRY: ENGLAND: United Kingdom
LANGUAGE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: English
ENTRY MONTH: Priority Journals
ENTRY WEEK: 199801
ENTRY WEEK: 19980104
AB Healthy humans have CD4+ T cells specific for self-components. Since autoreactive T cells in autoimmune patients may use a limited number of TCR V-region genes, we investigated here whether this also occurs for the potentially autoreactive CD4+ cells present in healthy persons. We studied CD4+ cells specific for human TSH receptor (TSHr) sequences, that are present with high frequency in healthy subjects and, as expected, in Graves' disease (GD) patients. We used short-term CD4+ cell lines propagated from four GD patients and five healthy subjects by cycles of stimulation with a pool of overlapping synthetic peptides corresponding to the putative extracellular parts of the TSHr sequence. The lines recognized the pool of TSHr peptides specifically and vigorously. Their epitope repertoire had been characterized previously: each line recognized one or a few TSHr peptides, different for each subject. We determined their TCR Vbeta usage by a semi-quantitative reverse transcriptase PCR assay, using primers specific for each known human Vbeta region family, in conjunction with a constant region primer. Six lines preferentially used one Vbeta family (42-94%), different for each line. In all lines, three or less Vbeta families accounted for approximately 60% or more of the Vbeta usage. Different Vbeta regions were used by each subject. There was no obvious difference between the Vbeta usage of the lines from GD patients and healthy controls. These results suggest that a limited pool of potentially autoreactive T cells survives clonal deletion. The pathogenic CD4+ cells involved in autoimmune diseases are likely recruited from that pool, since they have similar characteristics of epitope and TCR repertoire as the CD4+ cells specific for the same autoantigen in healthy subjects. Copyright 1997 Academic Press Limited.

L11 ANSWER 11 OF 12 MEDLINE
ACCESSION NUMBER: 96202866 MEDLINE
DOCUMENT NUMBER: 96202866
TITLE: Analysis of T cell receptor beta chain repertoire in middle ear effusions.
AUTHOR: Takeuchi K; Fujita Y; Tomemori T; Yuta A; Iriyoshi N; Sakakura Y
CORPORATE SOURCE: Department of Otorhinolaryngology, Mie University School of Medicine, Tsu, Japan.
SOURCE: ANNALS OF OTOTOLOGY, RHINOLOGY AND LARYNGOLOGY, (1996 Mar) 105 (3) 213-7.
PUB. COUNTRY: Journal code: 5Q2. ISSN: 0003-4894.
PUB. COUNTRY: United States
LANGUAGE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: English
ENTRY MONTH: Abridged Index Medicus Journals; Priority Journals
ENTRY WEEK: 199608
AB In order to elucidate the immune response in otitis media with effusion (OME), the polymerase chain reaction was employed to examine T cells in middle ear effusions in patients with OME for utilization of T cell receptor (TCR) variable region genes. Specimens of RNA were

extracted from 13 ears of 12 patients (9 children and 3 adults). Oligonucleotide primers specific for individual TCR Vbeta gene families were used to amplify TCR gene products in each sample. Although the number of Vbeta families utilized by each sample varied from 1 family to 21, a few significant trends emerged. Eleven ears out of 13 expressed Vbeta7, which was the most frequently utilized (84.6%) Vbeta family among the 24 Vbeta families. In 5 of the 13 samples, the number of Vbeta families utilized was restricted to 1, which was Vbeta7 in all 5 samples. This result indicates the possibility that Vbeta7-bearing T cells in the middle ear are responding to a certain common antigen in some cases of OME.

L11 ANSWER 12 OF 12 MEDLINE
 ACCESSION NUMBER: 96421965 MEDLINE
 DOCUMENT NUMBER: 96421965
 TITLE: T-cell repertoire complexity after allogeneic bone marrow transplantation.
 AUTHOR: Roux E; Helg C; Chapuis B; Jeannet M; Roosnek E
 CORPORATE SOURCE: Division of Immunology, Department of Internal Medicine, Hôpital Cantonal Universitaire, Geneva, Switzerland.
 SOURCE: HUMAN IMMUNOLOGY, (1996 Jun-Jul) 48 (1-2) 135-8.
 PUB. COUNTRY: Journal code: G9W. ISSN: 0198-8859.
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199704
 ENTRY WEEK: 19970402

AB We analyzed the T-cell repertoire in patients transplanted with bone marrow from an HLA identical sibling by determining the TCR diversity through Vbeta-CDR3-size spectratyping with Vbeta/Cbeta- and Vbeta/Jbeta-specific primers. Using the Vbeta/Cbeta primers, we observed limited TCR diversity only in recipients of a T-cell-depleted graft, whereas the TCR diversity of patients transplanted with an unmanipulated graft seemed to be indistinguishable from the one of a normal individual. However, with Vbeta/Jbeta-specific primers, increase of the resolution by approximately 10-fold also allowed the detection of imbalances in the TCR repertoire of recipients of an unmanipulated graft. This demonstrates that when high numbers of T cells are cotransfused with marrow, the TCR repertoire is more complete but still not as complete as in normal individuals, thereby emphasizing the important role of coinfecting mature T cells in the restoration of the T-cell compartment after bone marrow transplantation.

=> s ky R?/au
 L12 1 KY R?/AU

=> s kay R?/au
 L13 2289 KAY R?/AU

=> s l13 and TCR
 L14 32 L13 AND TCR

=> dup rem l14
 PROCESSING COMPLETED FOR L14
 L15 18 DUP REM L14 (14 DUPLICATES REMOVED)

=> dis l15 1-18 ibib abs

L15 ANSWER 1 OF 18 MEDLINE DUPLICATE 1
 ACCESSION NUMBER: 2000429067 MEDLINE
 DOCUMENT NUMBER: 20384795
 TITLE: Antigen triggering selectively increases TCRBV gene transcription.
 AUTHOR: Lennon G P; Sillibourne J E; Furrie E; Doherty M J; Kay R A
 CORPORATE SOURCE: Department of Molecular and Cellular Pathology, University of Dundee, Ninewells Hospital and Medical School, Dundee, United Kingdom.
 SOURCE: JOURNAL OF IMMUNOLOGY, (2000 Aug 15) 165 (4) 2020-7.
 PUB. COUNTRY: Journal code: IFB. ISSN: 0022-1767.
 LANGUAGE: English
 FILE SEGMENT: Priority Journals; Abridged Index Medicus Journals
 ENTRY MONTH: 200011
 ENTRY WEEK: 20001103

AB When the TCR binds Ag it is phosphorylated, internalized, and degraded. We wished to examine whether this process was accompanied by a specific concomitant increase in TCR mRNA levels. To do this, PBMC and a T cell clone were cultured with a series of superantigens and an alloantigen. Only T cells specifically responding to an antigenic stimulus had increased levels of TCR beta-chain variable (TCRBV)-specific mRNA. This response was apparent after 48 h, peaked around 72 h, and was still elevated after 7 days. Increased gene transcription appeared to be driven solely by Ag as specific Ag depletion prevented culture supernatants transferring this effect. The level of TCRBV mRNA elevation was not influenced by the stimulating Ag, but appeared dependent on the gene encoding the stimulated TCR. Reporter gene assays, using cloned TCRBV gene promoters, confirmed both that TCR gene transcription rises after stimulation and that basal and stimulated levels of TCR transcription vary between different TCRBV genes. These data conclusively demonstrate that there is no direct relationship between TCRBV mRNA and T cell number, and that future repertoire studies must take both factors into account.

L15 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2001 ACS
 ACCESSION NUMBER: 1999:226584 CAPLUS
 DOCUMENT NUMBER: 130:236324
 TITLE: Sequence analysis of DA and Sprague Dawley rat T-cell receptor .beta.-chain promoters. [Erratum to document cited in CA130:109050]
 AUTHOR(S): Sillibourne, James E.; Kay, Richard A.
 CORPORATE SOURCE: Dep. Molecular and Cellular Pathology, Ninewells Hospital and Medical School, Dundee, DD1 9SY, UK
 SOURCE: Immunogenetics (1999), 49(3), 246
 PUBLISHER: CODEN: IMNGBK; ISSN: 0093-7711
 DOCUMENT TYPE: Springer-Verlag
 LANGUAGE: English

AB Figs. 1 and 2 of this Sequence Register article were incorrect as

originally printed; the correct versions are given.

L15 ANSWER 3 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:154413 BIOSIS
DOCUMENT NUMBER: PREV200000154413
TITLE: The duodecamer motif is critical for both basal and stimulated TCRBV promoter function.
AUTHOR(S): Doherty, M. J. (1); Lennon, G. P. (1); Sillibourne, J. E. (1); Furrie, E. (1); Kay, R. A. (1)
CORPORATE SOURCE: (1) Dept. Molecular and Cellular Pathology, University of Dundee, Dundee, DD1 9SY UK
SOURCE: Immunology., (Dec., 1999) Vol. 98, No. suppl. 1, pp. 123. Meeting Info.: Joint Congress of the British Society for Immunology and the British Society for Allergy & Clinical Immunology. Harrogate, England, UK November 30-December 03, 1999 British Society for Allergy & Clinical Immunology . ISSN: 0019-2805.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L15 ANSWER 4 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:139956 BIOSIS
DOCUMENT NUMBER: PREV200000139956
TITLE: The TCRBV13 TCR repertoire in anti-52 KDA Ro autoantibody-positive Sjogren's syndrome.
AUTHOR(S): Furrie, E. (1); Doherty, M. J. (1); Kershaw, A.; Crighton, A. J.; Morley, K.; Kay, R. A. (1)
CORPORATE SOURCE: (1) Dept. Molecular and Cellular Pathology, University of Dundee, Dundee, DD1 9SY UK
SOURCE: Immunology., (Dec., 1999) Vol. 98, No. suppl. 1, pp. 33. Meeting Info.: Joint Congress of the British Society for Immunology and the British Society for Allergy and Clinical Immunology. Harrogate, England, UK November 30-December 03, 1999 British Society for Allergy and Clinical Immunology . ISSN: 0019-2805.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L15 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:795052 CAPLUS
DOCUMENT NUMBER: 130:37286
TITLE: Immunological method
INVENTOR(S): Kay, Richard Andrew
PATENT ASSIGNEE(S): University of Dundee, UK
SOURCE: PCT Int. Appl., 77 pp. CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9854223	A2	19981203	WO 1998-GB1382	19980527
WO 9854223	A3	19990304		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9876631	A1	19981230	AU 1998-76631	19980527
AU 728909	B2	20010118		
EP 1017724	A2	20000712	EP 1998-924427	19980527
R: CH, DE, FR, GB, IT, LI, NL, SE				
PRIORITY APPLN. INFO.: GB 1997-10820 19970527				
WO 1998-GB1382 19980527				
AB A method of identifying an antigen-responsive T cell within a population of T cells, the method comprising the steps of: (1) obtaining a sample contg. T cells which have responded to the antigen; (2) detg. individually for each of a plurality of specific T cell receptors, or individually for each of a plurality of subsets of T cell receptors, whether expression of a gene encoding a specific T cell receptor, or whether expression of genes encoding a subset of T cell receptors, has increased per specific T cell receptor-pos. T cell or per specific T cell receptor-pos. T cell subset compared to the expression of said gene or genes in a sample contg. T cells which have not responded to the antigen. The method is useful for identifying antigen-responsive T cells which are assocd. with a disease state such as rheumatoid arthritis.				

L15 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:683257 CAPLUS
DOCUMENT NUMBER: 130:109050
TITLE: Sequence analysis of DA and Sprague Dawley rat T-cell receptor .beta.-chain promoters
AUTHOR(S): Sillibourne, James E.; Kay, Richard A.
CORPORATE SOURCE: Department of Molecular and Cellular Pathology, Ninewells Hospital and Medical School, Dundee, DD1 9SY, UK
SOURCE: Immunogenetics (1998), 48(5), 356-358
CODEN: IMNGBK; ISSN: 0093-7711
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The genomic sequences of 4 rat TCR .beta.-chain genes were analyzed in 1 inbred (DA) and 1 outbred (Sprague Dawley) rat strains. The sequences suggest that these promoters are capable of binding a comprehensive range of lineage-specific and non-lineage-specific factors, including putative binding sites for AP-1, AP-2, Spl, GATA-binding factors, CREB, Ets-1, LEF-1, AML-1, and TCF-1. CAAT and TATA boxes were also identified in some of the promoters.

REFERENCE COUNT: 6
REFERENCE(S): (1) Halle, J; Mol Cell Biol 1997, V17, P4220 CAPLUS
(2) Kay, R; Eur J Immunol 1994, V24, P2863 CAPLUS
(3) Li, Y; J Exp Med 1991, V174, P1537 CAPLUS
(5) Rowen, L; Science 1996, V272, P1755 CAPLUS
(6) Smith, L; J Immunol 1991, V147, P375 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 7 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS
 ACCESSION NUMBER: 1999:125347 BIOSIS
 DOCUMENT NUMBER: PREV199900125347
 TITLE: Superantigens increase specific TCR gene transcription rates in unseparated human lymphocyte populations.
 AUTHOR(S): Lennon, Greig; Sillibourne, James; Kay, Richard
 CORPORATE SOURCE: Univ. Dep. Molecular Cellular Pathol., Ninewells Hosp. Med. Sch., Dundee DD1 9SY UK
 SOURCE: Immunology, (Dec., 1998) Vol. 95, No. SUPPL. 1, pp. 28. Meeting Info.: 6th Annual Congress of the British Society for Immunology Harrogate, England, UK December 1-4, 1998 ISSN: 0019-2805.
 DOCUMENT TYPE: Conference
 LANGUAGE: English

L15 ANSWER 8 OF 18 MEDLINE DUPLICATE 2
 ACCESSION NUMBER: 97414173 MEDLINE
 DOCUMENT NUMBER: 97414173
 TITLE: Long-term alloreactive T cell lines and clones express a limited T cell receptor repertoire.
 AUTHOR: Tavakoli Afshari J; Hutchinson I V; Kay R A
 CORPORATE SOURCE: School of Biological Sciences, University of Manchester, UK.
 SOURCE: TRANSPLANT IMMUNOLOGY, (1997 Jun) 5 (2) 122-8. Journal code: B32. ISSN: 0966-3274.
 PUB. COUNTRY: ENGLAND: United Kingdom
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199801
 ENTRY WEEK: 19980104

AB Alloreactive T cells recognize either determinants of the intact donor MHC molecules displayed on the surface of transplanted-cells or peptide fragments of donor antigens associated with self-MHC molecules by means of their T cell receptors (TCR). To investigate the relationship between the TCR beta chain structure and allorecognition, we established and characterized four long-term T cell lines and seven T cell clones derived following a mixed lymphocyte reaction (MLR) between fully histoincompatible DA (RT1a) and LEW (RT1(l)) rat lymph node cells. These DA anti-LEW T cells were phenotypically CD4+, CD8-, alpha beta TCR + and produced interferon-gamma but not IL-4, consistent with being Th1 CD4+ T cells. As might be expected, these cells were not significantly cytotoxic and did not display suppressor activity. Analysis of the TCR beta chain gene structure revealed a very restricted repertoire in both long-term lines and clones. The TCRBV6S1 gene was present in 15/21 of the alloreactive T cell mRNA transcripts but only 1/12 of unstimulated DA splenic TCR mRNA transcripts (p = 0.0018). Similarly, the TCRBJ2S1 gene was also used frequently in the alloreactive transcripts (17/21) but in only 2/12 unstimulated splenic transcripts (p = 0.0013). Furthermore, all 15 of the alloreactive TCRBV6S1 transcripts had a distinctive four amino acid N region motif not present in any of the unstimulated TCR transcripts (p = 0.0003). These experiments reveal a distinct homogeneity amongst stable allogeneic T cells in culture. If these results reflect the situation in vivo, the possibility exists that specific immunotherapy may be successful in preventing allograft rejection.

L15 ANSWER 9 OF 18 MEDLINE DUPLICATE 3
 ACCESSION NUMBER: 96132972 MEDLINE
 DOCUMENT NUMBER: 96132972
 TITLE: Reduction of early B lymphocyte precursors in transgenic mice overexpressing the murine heat-stable antigen.
 AUTHOR: Hough M R; Chappel M S; Sauvageau G; Takei F; Kay R ; Humphries R K
 CORPORATE SOURCE: Terry Fox Laboratory, British Columbia Cancer Agency, Vancouver, Canada.
 SOURCE: JOURNAL OF IMMUNOLOGY, (1996 Jan 15) 156 (2) 479-88. Journal code: IFB. ISSN: 0022-1767.
 PUB. COUNTRY: United States
 LANGUAGE: English
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
 ENTRY MONTH: 199604

AB To study the role of the murine heat-stable Ag (HSA) in lymphocyte maturation, we generated transgenic mice in which the HSA cDNA was under the transcriptional control of the TCR V beta promoter and Ig mu enhancer. The HSA transgene was expressed during all stages of B lymphocyte maturation. Expression was first detected in the earliest lymphoid-committed progenitors, which normally do not express HSA, and subsequently reached the highest levels in pro- and pre-B cells. In bone marrow, the number of IL-7-responsive clonogenic progenitors was < 4% of normal, whereas the frequency of earlier B lymphocyte-restricted precursors, detectable as Whitlock-Witte culture-initiating cells, was normal. Pro- and pre-B cells detected by flow cytometry were reduced by approximately 50% relative to controls. Mature splenic B cells were also reduced but to a lesser extent than in marrow, and their response to LPS stimulation was impaired. Reconstitution of SCID and BALB/c-nu/nu mice with HSA transgenic marrow indicated that the perturbations in B lymphopoiesis were not caused by a defective marrow microenvironment or by abnormal T cells. Our previous studies showed elevated HSA expression throughout thymocyte development, which resulted in a profound depletion of CD4+CD8+ double-positive and single-positive thymocytes. Together, these results indicate that HSA levels can determine the capacity of early T and B lymphoid progenitors to proliferate and survive. Therefore, HSA could serve as an important regulator during the early stages of B and T lymphopoiesis.

L15 ANSWER 10 OF 18 MEDLINE DUPLICATE 4
 ACCESSION NUMBER: 96303221 MEDLINE
 DOCUMENT NUMBER: 96303221
 TITLE: TCR gene polymorphisms and autoimmune disease.
 AUTHOR: Kay R A
 CORPORATE SOURCE: Department of Pathology, Ninewells Hospital & Medical School, Dundee, UK.
 SOURCE: EUROPEAN JOURNAL OF IMMUNOGENETICS, (1996 Apr) 23 (2) 161-77. Ref: 129. Journal code: AZ6. ISSN: 0960-7420.
 PUB. COUNTRY: ENGLAND: United Kingdom
 LANGUAGE: English
 FILE SEGMENT: Journal; Article; (JOURNAL ARTICLE)
 ENTRY MONTH: 199604
 ENTRY WEEK: 19960104

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612

AB Autoimmunity may result from abnormal regulation within the immune system. As the T cell is the principal regulator of the immune system and its normal function depends on immune recognition or self/non-self discrimination, abnormalities of the idiotypic T-cell receptor (TCR) may be one cause of autoimmune disease. The TCR is a clonally distributed, cell-surface heterodimer which binds peptide antigen when complexed with HLA molecules. In order to recognize the variety of antigens it may possibly encounter, the TCR, by necessity, is a diverse structure. As with immunoglobulin, it is the variable domain of the TCR which interacts with antigen and exhibits the greatest amount of amino acid variability. The underlying genetic basis for this structural diversity is similar to that described for immunoglobulin, with TCR diversity relying on the somatic recombination, in a randomly imprecise manner, of smaller gene segments to form a functional gene. There are a large number of gene segments to choose from (particularly the TCRAV, TCRAJ and TCRBV gene segments) and some of these also exhibit allelic variation. Finally, polymorphisms in non-coding regions of TCR genes, leading to biased recombination or expression, are also beginning to be recognized. All these factors contribute to the polymorphic nature of the TCR, in terms of both structure and repertoire formation. It follows that inherited abnormalities in either coding or regulatory regions of TCR genes may predispose to aberrant T-cell function and autoimmune disease. This review will outline the genomic organization of the TCR genes, the genetic mechanisms responsible for the generation of diversity, and the results of investigations into the association between germline polymorphisms and autoimmune disease.

L15 ANSWER 11 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1995:384429 BIOSIS
DOCUMENT NUMBER: PREV199598398729
TITLE: Limited heterogeneity of TCR V-beta gene utilisation by alloreactive T cells.
AUTHOR(S): Tavakoli, J.; Hutchinson, I. V.; Kay, R.
CORPORATE SOURCE: Univ. Manchester, Med. Sch., Manchester M13 9PT UK
SOURCE: 9TH INTERNATIONAL CONGRESS OF IMMUNOLOGY.. (1995) pp. 646. The 9th International Congress of Immunology. Publisher: 9th International Congress of Immunology San Francisco, California, USA.
Meeting Info.: Meeting Sponsored by the American Association of Immunologists and the International Union of Immunological Societies San Francisco, California, USA July 23-29, 1995
DOCUMENT TYPE: Conference
LANGUAGE: English

L15 ANSWER 12 OF 18 MEDLINE DUPLICATE 5

ACCESSION NUMBER: 96023322 MEDLINE
DOCUMENT NUMBER: 96023322
TITLE: A subset of Sjogren's syndrome associates with the TCRBV13S2 locus but not the TCRBV2S1 locus.
AUTHOR: Kay R A; Hutchings C J; Ollier W E
CORPORATE SOURCE: Immunology Research Group, University of Manchester, United Kingdom..
SOURCE: HUMAN IMMUNOLOGY, (1995 Apr) 42 (4) 328-30. Journal code: G9W. ISSN: 0198-8859.
PUB. COUNTRY: United States
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199601

AB HGPSS associates with the TCRBV6S7 locus within the TCR beta-chain gene complex. However, V beta 6.7 T cells, encoded by this locus, have never been implicated in the salivary gland destruction that characterizes primary Sjogren's syndrome. Both V beta 13 and V beta 2 T cells have been implicated in glandular destruction. We therefore analyzed the association of HGPSS with both TCRBV2S1, the only TCRBV2 locus, and the TCRBV13S2 locus (the TCRBV13 family member which lies closest to TCRBV6S7). Our results show that the prevalence of TCRBV13S2*2 homozygotes is significantly increased in HGPSS and that there is a high degree of linkage disequilibrium between this locus and TCRBV6S7 not previously described across the TCR beta-chain gene complex. However, HGPSS does not associate with the TCRBV2S1 locus. These results suggest that it is the V beta 13.2 T cell which may be responsible for the autoimmune destruction that characterizes HGPSS and that the previous association of this condition with the TCRBV6S7 locus is primary due to the linkage disequilibrium that exists between it and TCRBV13S2.

L15 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1995:204308 CAPLUS
DOCUMENT NUMBER: 122:184945
TITLE: Genetic control of the human V.beta.13.2 T cell repertoire: importance of allelic variation outside the coding regions of the TCRBV13S2 gene
AUTHOR(S): Kay, Richard A.; Snowden, Neil; Hajeer, Ali H.; Boylston, Art W.; Ollier, William E. R.
CORPORATE SOURCE: Immunology Research Group, Univ. Manchester, Leeds, UK
SOURCE: Eur. J. Immunol. (1994), 24(11), 2863-7
CODEN: EJIMAF; ISSN: 0014-2980
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In humans, the T cell repertoire is influenced by HLA, T cell receptor null alleles and antigen. Here, the authors describe a novel mechanism, independent of superantigen or T cell receptor structure which influences the T cell repertoire in a V.beta.-dependent manner. The authors have identified a biallelic locus, the TCRBV13S2 T cell receptor gene, where allelic differences predominate in the non-coding regions including transitions, transversions and frameshift deletions. The expressed protein is non-polymorphic at this locus. The TCRBV13S2 genotype profoundly influences the circulating level of V.beta.13.2 CD4 T cells but does not affect T cell receptor expression or function.

L15 ANSWER 14 OF 18 MEDLINE

ACCESSION NUMBER: 95135387 MEDLINE
DOCUMENT NUMBER: 95135387
TITLE: [Idiotypic T-lymphocyte receptor in animal and human autoimmune diseases].
Le recepteur idiotypique des lymphocytes T dans les maladies auto-immunes animales et humaines.
AUTHOR: Kay R A; Ollier W E

CORPORATE SOURCE: ACR Epidemiology Research Unit, Manchester, Grande Bretagne, UK..

SOURCE: REVUE DU RHUMATISME. EDITION FRANCAISE, (1994) 61 (7-8) 532-45. Ref: 147
Journal code: BQU.

PUB. COUNTRY: France
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LANGUAGE: French

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199505

AB Animal models have demonstrated that the T-cell repertoire is restricted when the response to defined autoantigens is studied. Anti-V beta specific monoclonal antibodies or specific V beta-derived peptides can be used to manipulate autoreactive T-cells to either prevent or treat established experimental disease in animals. In some animal models of arthritis, inherited differences in the TCR repertoire can protect against the development of experimental autoimmune disease. Human studies have generally given conflicting results with regard to the role of the TCR complexes as susceptibility loci for disease. This may be due to the heterogeneity present in the human population and/or in the diseases studied. In some diseases, where there is convincing evidence for putative autoantigens (multiple sclerosis) or distinct immunodysfunctional pathology (hypergammaglobulinaemic primary Sjogren's syndrome), restricted TCR repertoires and germline TCR susceptibility loci can be discerned. Recent evidence suggests that autoimmune disease may eventually be mapped to regulatory regions of the TCR V genes rather than the allelic differences in coding region structure. This may have implications for the future therapy of autoimmune rheumatic disease.

L15 ANSWER 15 OF 18 MEDLINE

ACCESSION NUMBER: 95135386 MEDLINE

DOCUMENT NUMBER: 95135386

TITLE: [T-lymphocyte receptor genes: genome organization and genetic mechanisms of repertoire diversity].
G'enes du recepteur des lymphocytes T: organisation genomique et mecanismes genetiques de la diversite du repertoire.

AUTHOR: Kay R A; Ollier W E

CORPORATE SOURCE: ACR Epidemiology Research Unit, Manchester, UK..

SOURCE: REVUE DU RHUMATISME. EDITION FRANCAISE, (1994) 61 (7-8) 521-31. Ref: 104
Journal code: BQU.

PUB. COUNTRY: France
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LANGUAGE: French

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199505

AB The T-cell receptor (TCR) is fundamental to the immune process in both health and disease. Reviewed here is the genetic organisation of the gene complexes which encode the TCR polypeptide chains alpha, beta, gamma, and delta. The TCR is by necessity a diverse structure and we consider the genetic mechanisms responsible for this. These include multiple variable gene segment isotypes, somatic recombination of gene segments, imprecisions in the recombination process and allelic variations in gene segments structure and regulation.

L15 ANSWER 16 OF 18 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 94298865 EMBASE

DOCUMENT NUMBER: 1994298865

TITLE: Idiotypic T-cell receptor studies in animal and human autoimmune disease.

AUTHOR: Kay R.A.; Ollier W.E.R.

CORPORATE SOURCE: ACR Epidemiology Research Unit, Oxford Road, Manchester M13 9PT, United Kingdom

SOURCE: Revue du Rhumatisme (English Edition), (1994) 61/7-8 (470-482).
ISSN: 1169-8446 CODEN: RRHUEX

COUNTRY: France

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 006 Internal Medicine
026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism

LANGUAGE: English

SUMMARY LANGUAGE: English; French

AB Animal models have demonstrated that the T-cell repertoire is restricted when the response to defined autoantigens is studied. Anti-V.beta. specific monoclonal antibodies or specific V.beta.-derived peptides can be used to manipulate autoreactive T-cells to either prevent or treat established experimental disease in animals. In some animal models of arthritis, inherited differences in the TCR repertoire can protect against the development of experimental autoimmune disease. Human studies have generally given conflicting results with regard to the role of the TCR complexes as susceptibility loci for disease. This may be due to the heterogeneity present in the human population and/or in the diseases studied. In some diseases, where there is convincing evidence for putative autoantigens (multiple sclerosis) or distinct immunodysfunctional pathology (hypergammaglobulinaemic primary Sjogren's syndrome), restricted TCR repertoires and germline TCR susceptibility loci can be discerned. Recent evidence suggests that autoimmune disease may eventually be mapped to regulatory regions of the TCR V genes rather than the allelic differences in coding region structure. This may have implications for the future therapy of autoimmune rheumatic disease.

L15 ANSWER 17 OF 18 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 94298864 EMBASE

DOCUMENT NUMBER: 1994298864

TITLE: The T-cell receptor genes: Genomic organisation and the genetic basis of repertoire diversity.

AUTHOR: Kay R.A.; Ollier W.E.R.

CORPORATE SOURCE: ACR Epidemiology Research Unit, Oxford Road, Manchester M13 9PT, United Kingdom

SOURCE: Revue du Rhumatisme (English Edition), (1994) 61/7-8 (459-469).
ISSN: 1169-8446 CODEN: RRHUEX

COUNTRY: France

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 006 Internal Medicine
026 Immunology, Serology and Transplantation

031 Arthritis and Rheumatism

LANGUAGE: English
SUMMARY LANGUAGE: English; French

AB The T-cell receptor (TCR) is fundamental to the immune process in both health and disease. Reviewed here is the genetic organisation of the gene complexes which encode the TCR polypeptide chains .alpha., .beta., .gamma. and .delta.. The TCR is by necessity a diverse structure and we consider the genetic mechanisms responsible for this. These include multiple variable gene segment isotypes, somatic recombination of gene segments, imprecisions in the recombination process and allelic variations in gene segment structure and regulation.

L15 ANSWER 18 OF 18 MEDLINE

DUPLICATE 6

ACCESSION NUMBER: 91322881 MEDLINE

DOCUMENT NUMBER: 91322881

TITLE: An abnormal T cell repertoire in hypergammaglobulinaemic primary Sjogren's syndrome.

AUTHOR: Kay R A; Hay E M; Dyer P A; Dennett C; Green L M; Bernstein R M; Holt P J; Pumphrey R S; Boylston A W; Ollier W E

CORPORATE SOURCE: Regional Immunology Service, St Mary's Hospital, Manchester, UK..

SOURCE: CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1991 Aug) 85 (2) 262-4.

PUB. COUNTRY: Journal code: DD7. ISSN: 0009-9104.

ENGLAND: United Kingdom

LANGUAGE: Journal; Article; (JOURNAL ARTICLE)

FILE SEGMENT: English

ENTRY MONTH: Priority Journals; Cancer Journals

ENTRY MONTH: 199111

AB T cell antigen specificity is determined by the products of the genes which encode the variable regions of their receptors. Of the T cell receptor (TCR) variable region gene products examined, only V beta 6.7a TCR-positive lymphocytes were reduced in primary Sjogren's syndrome patients with IgG1 hypergammaglobulinaemia compared with an age-, sex- and HLA-matched control population. The levels of V beta 6.7a T cells were also significantly reduced when these patients were compared with an age- and sex-matched but HLA-unmatched control group and non-tissue typed normal people of both sexes. Since published studies show no such abnormality in rheumatoid arthritis, systemic lupus erythematosus or other autoimmune diseases, this abnormality may reflect a pathogenic process specific to primary Sjogren's syndrome.

=> end

ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF

LOGOFF? (Y)/N/HOLD:y

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
97.81	97.96

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
-4.70	-4.70

CA SUBSCRIBER PRICE

STN INTERNATIONAL LOGOFF AT 11:00:24 ON 18 APR 2001

=> s TCR and ((degenerate or generic) (5N) primer?)
L1 55 TCR AND ((DEGENERATE OR GENERIC) (5N) PRIMER?)

=> dup rem l1
PROCESSING COMPLETED FOR L1
L2 17 DUP REM L1 (38 DUPLICATES REMOVED)

=> dis l2 1-17 ibibi abs kwic
'IBIBI' IS NOT A VALID FORMAT
In a multifile environment, a format can only be used if it is valid
in at least one of the files. Refer to file specific help messages
or the STNGUIDE file for information on formats available in
individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):end

=> dis l2 1-17 ibib abs kwic

L2 ANSWER 1 OF 17 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001099135 MEDLINE
DOCUMENT NUMBER: 20565479
TITLE: T-cell antigen receptors in Atlantic cod (Gadus morhua L.):
structure, organisation and expression of TCR
alpha and beta genes.
AUTHOR: Wermerstam N E; Pilstrom L
CORPORATE SOURCE: Immunology Programme, Department of Cell and Molecular
Biology, BMC, Uppsala University, Box 596, S-751 24,
Uppsala, Sweden.
SOURCE: DEVELOPMENTAL AND COMPARATIVE IMMUNOLOGY, (2001 Mar) 25 (2)
117-35.
PUB. COUNTRY: Journal code: E3M. ISSN: 0145-305X.
United States
LANGUAGE: Journal; Article; (JOURNAL ARTICLE)
English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AJ133844; GENBANK-AJ133845; GENBANK-AJ133846;
GENBANK-AJ133847; GENBANK-AJ133848; GENBANK-AJ133849;
GENBANK-AJ133850; GENBANK-AJ133851
ENTRY MONTH: 200102

AB By using short **degenerate primers** complementing
conserved T-cell antigen receptor (TCR) variable and constant
region segments for PCR, we were able to isolate putative TCRalpha and
beta chain full length cDNAs in Atlantic cod. The Valpha and Vbeta domains
have the canonical features of known teleost and mammalian TCR V
domains, including conserved residues in the beginning of FR2 and at the
end of FR3. The Jalpha and Jbeta region possess the conserved
Phe-Gly-X-Gly motif found in nearly all TCR and immunoglobulin
light chain J regions. Similar to other vertebrates, the Atlantic cod
Calpha and Cbeta sequences exhibit distinct immunoglobulin, connecting
peptide, transmembrane and cytoplasmic regions. The Atlantic cod Cbeta
sequence lacks a cysteine in its connecting peptide region, but other
motifs proposed to be important for dimerisation and cell surface
expression are observed. Four different cod Cbeta sequences were
identified, two of which share 3' untranslated regions different from one
of the other two sequences, suggesting the existence of isotypic gene
variants of Cbeta. Based on Southern blot analyses, the TCRalpha and beta
gene loci appear to be arranged in translocon organisation (as opposed to
multiclustler) with multiple V gene segments, some (D) and J gene segments
and a single or few C gene segments. Northern blot analyses show
expression of the TCRalpha and beta chains in thymus, spleen and head
kidney, expression of the TCRbeta chain was also detected in the ovary.
Interestingly, no expression was detected in intestine even though the
existence of T-cells in intestine has been proposed in other teleost
species.

TI T-cell antigen receptors in Atlantic cod (Gadus morhua L.): structure,
organisation and expression of TCR alpha and beta genes.

AB By using short **degenerate primers** complementing
conserved T-cell antigen receptor (TCR) variable and constant
region segments for PCR, we were able to isolate putative TCRalpha and
beta chain full length cDNAs in Atlantic cod. The Valpha and Vbeta domains
have the canonical features of known teleost and mammalian TCR V
domains, including conserved residues in the beginning of FR2 and at the
end of FR3. The Jalpha and Jbeta region possess the conserved
Phe-Gly-X-Gly motif found in nearly all TCR and immunoglobulin
light chain J regions. Similar to other vertebrates, the Atlantic cod
Calpha and Cbeta sequences exhibit distinct immunoglobulin,...

L2 ANSWER 2 OF 17 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2000171513 MEDLINE
DOCUMENT NUMBER: 20171513
TITLE: Description of an ectothermic TCR coreceptor, CD8
alpha, in rainbow trout.
AUTHOR: Hansen J D; Strassburger P
CORPORATE SOURCE: Basel Institute for Immunology, Basel, Switzerland..
hansen@bii.ch
SOURCE: JOURNAL OF IMMUNOLOGY, (2000 Mar 15) 164 (6) 3132-9.
Journal code: IFB. ISSN: 0022-1767.
PUB. COUNTRY: United States
LANGUAGE: Journal; Article; (JOURNAL ARTICLE)
English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer
Journals
OTHER SOURCE: GENBANK-AF178053; GENBANK-AF178054; GENBANK-AF178055
ENTRY MONTH: 200006
ENTRY WEEK: 20000601

AB We have cloned the first CD8 alpha gene from an ectothermic source using a
degenerate primer for Ig superfamily V domains. Similar
to homologues in higher vertebrates, the rainbow trout CD8 alpha gene
encodes a 204-aa mature protein composed of two extracellular domains
including an Ig superfamily V domain and hinge region. Differing from
mammalian CD8 alpha V domains, lower vertebrate (trout and chicken)
sequences do not contain the extra cysteine residue (C strand) involved in
the abnormal intrachain disulfide bridging within the CD8 alpha V domain
of mice and rats. The trout membrane proximal hinge region contains the
two essential cysteine residues involved in CD8 dimerization (alpha alpha
or alpha beta) and threonine, serine, and proline residues which may be
involved in multiple O-linked glycosylation events. Although the
transmembrane region is well conserved in all CD8 alpha sequences analyzed
to date, the putative trout cytoplasmic region differs and, in fact, lacks
the consensus p56lck motif common to other CD8 alpha sequences. We then
determined that the trout CD8 alpha genomic structure is similar to that
of humans (six exons) but differs from that of mice (five exons).

Additionally, Northern blotting and RT-PCR demonstrate that trout CD8 alpha is expressed at high levels within the thymus and at weaker levels in the spleen, kidney, intestine, and peripheral blood leukocytes. Finally, we show that trout CD8 alpha can be expressed on the surface of cells via transfection. Together, our results demonstrate that the basic structure and expression of CD8 alpha has been maintained for more than 400 million years of evolution.

TI Description of an ectothermic TCR coreceptor, CD8 alpha, in rainbow trout.
 AB We have cloned the first CD8 alpha gene from an ectothermic source using a degenerate primer for Ig superfamily V domains. Similar to homologues in higher vertebrates, the rainbow trout CD8 alpha gene encodes a 204-aa.

L2 ANSWER 3 OF 17 MEDLINE . DUPLICATE 3
 ACCESSION NUMBER: 2000411646 MEDLINE
 DOCUMENT NUMBER: 20394656
 TITLE: Immunopurification of T-cells from sea bass *Dicentrarchus labrax* (L.).
 AUTHOR: Scapigliati G; Romano N; Abelli L; Meloni S; Ficca A G; Buonocore F; Bird S; Secombes C J
 CORPORATE SOURCE: Dipartimento di Scienze Ambientali, Universita della Tuscia, Viterbo, Italy.. scapigg@unitus.it
 SOURCE: Fish Shellfish Immunol. (2000 May) 10 (4) 329-41.
 PUB. COUNTRY: Journal code: DR8. ISSN: 1050-4648.
 ENGLAND: United Kingdom
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200011
 ENTRY WEEK: 20001101

AB The monoclonal antibody DLT15, specific for thymocytes and peripheral T-cells of the teleost fish *Dicentrarchus labrax* (sea bass), was used to purify immunoreactive cells from blood and gut-associated lymphoid tissue. The purification was performed by immuno-magnetic sorting of leucocyte fractions enriched by Percoll density gradient centrifugation, and the purity of the isolated cells was estimated by cytofluorimetric analysis. Following a single step, the percentage of DLT15-purified cells was 88 +/- 10% for gut-associated lymphoid tissue and 79 +/- 18% for blood leucocytes. DLT15-purified cells from gut-associated lymphoid tissue were employed for RNA extraction and cDNA synthesis. In RT-PCR experiments using as primers degenerate oligonucleotides corresponding to the peptide sequence MYWY and VYFCA of the trout TcR beta chain, a 203 bp product was amplified. When sequenced, the cDNA was found to show 60% nucleotide identity to the trout TcRV beta 3. By 3'-RACE the cDNA was elongated to obtain the TcR constant region, with high similarity to other fish TcR sequences. These results strongly suggest that cells recognised by DLT15 are putative T lymphocytes.

AB . . . leucocytes. DLT15-purified cells from gut-associated lymphoid tissue were employed for RNA extraction and cDNA synthesis. In RT-PCR experiments using as primers degenerate oligonucleotides corresponding to the peptide sequence MYWY and VYFCA of the trout TcR beta chain, a 203 bp product was amplified. When sequenced, the cDNA was found to show 60% nucleotide identity to the trout TcRV beta 3. By 3'-RACE the cDNA was elongated to obtain the TcR constant region, with high similarity to other fish TcR sequences. These results strongly suggest that cells recognised by DLT15 are putative T lymphocytes.

L2 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 4
 ACCESSION NUMBER: 2000:853499 CAPLUS
 TITLE: T-cell antigen receptors in Atlantic cod (*Gadus morhua* L.): structure, organisation and expression of TCR .alpha. and .beta. genes
 AUTHOR(S): Wermerstam, N. E.; Pilstrom, L.
 CORPORATE SOURCE: BMC, Department of Cell and Molecular Biology, Immunology Programme, Uppsala University, Uppsala, S-751 24, Swed.
 SOURCE: Dev. Comp. Immunol. (2000), 25(2), 117-135
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB By using short degenerate primers complementing conserved T-cell antigen receptor (TCR) variable and const. region segments for PCR, we were able to isolate putative TCR .alpha. and .beta. chain full length cDNAs in Atlantic cod. The V.alpha. and V.beta. domains have the canonical features of known teleost and mammalian TCR V domains, including conserved residues in the beginning of FR2 and at the end of FR3. The J.alpha. and J.beta. region possess the conserved Phe-Gly-X-Gly motif found in nearly all TCR and Ig light chain J regions. Similar to other vertebrates, the Atlantic cod C.alpha. and C.beta. sequences exhibit distinct Ig, connecting peptide, transmembrane and cytoplasmic regions. The Atlantic cod C.beta. sequence lacks a cysteine in its connecting peptide region, but other motifs proposed to be important for dimerization and cell surface expression are obsd. Four different cod C.beta. sequences were identified, two of which share 3' untranslated regions different from one of the other two sequences, suggesting the existence of isotypic gene variants of C.beta.. Based on Southern blot analyses, the TCR .alpha. and .beta. gene loci appear to be arranged in translocon organization (as opposed to multicluster) with multiple V gene segments, some (D) and J gene segments and a single or few C gene segments. Northern blot analyses show expression of the TCR.alpha. and .beta. chains in thymus, spleen and head kidney, expression of the TCR.beta. chain was also detected in the ovary. Interestingly, no expression was detected in intestine even though the existence of T-cells in intestine has been proposed in other teleost species.

REFERENCE COUNT: 57
 REFERENCE(S):
 (2) Alcover, A; J Biol Chem 1990, V265, P4131 CAPLUS
 (3) Arnaud, J; Int Immunol 1997, V9, P615 CAPLUS
 (5) Backstrom, B; Science 1998, V281, P835 CAPLUS
 (6) Bengten, E; Dev Comp Immunol 1994, V18, P109 CAPLUS
 (7) Bengten, E; Eur J Immunol 1991, V21, P3027 CAPLUS

TI T-cell antigen receptors in Atlantic cod (*Gadus morhua* L.): structure, organisation and expression of TCR .alpha. and .beta. genes

AB By using short degenerate primers complementing conserved T-cell antigen receptor (TCR) variable and const. region segments for PCR, we were able to isolate putative TCR

.alpha. and .beta. chain full length cDNAs. The V.alpha. and V.beta. domains have the canonical features of known teleost and mammalian TCR V domains, including conserved residues in the beginning of FR2 and at the end of FR3. The J.alpha. and J.beta. region possess the conserved Phe-Gly-X-Gly motif found in nearly all TCR and Ig light chain J regions. Similar to other vertebrates, the Atlantic cod C.alpha. and C.beta. sequences exhibit distinct Ig, connecting peptide, transmembrane and cytoplasmic regions. The Atlantic cod C.beta. sequence lacks a cysteine in its connecting peptide region, but other motifs proposed to be important for dimerization and cell surface expression are observed. Four different cod C.beta. sequences were identified, two of which share 3' untranslated regions different from one of the other two sequences, suggesting the existence of isotypic gene variants of C.beta.. Based on Southern blot analyses, the TCR .alpha. and .beta. gene loci appear to be arranged in translocon organization (as opposed to multicluster) with multiple V gene segments, some (D) and J gene segments and a single or few C gene segments. Northern blot analyses show expression of the TCR.alpha. and .beta. chains in thymus, spleen and head kidney, expression of the TCR.beta. chain was also detected in the ovary. Interestingly, no expression was detected in intestine even though the existence of T-cells in intestine has been proposed in other teleost species.

L2 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1998:151255 CAPLUS
DOCUMENT NUMBER: 128:214967
TITLE: RAFTK (related adhesion focal tyrosine kinase)
molecules involved in regulation of cellular processes
and the genes encoding them
INVENTOR(S): Avraham, Shalom; Avraham, Hava; Groopman, Jerome E.
PATENT ASSIGNEE(S): Beth Israel Deaconess Medical Center, Inc., USA
SOURCE: PCT Int. Appl., 168 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9807870	A1	19980226	WO 1997-US14093	19970812
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9741479	A1	19980306	AU 1997-41479	19970812
US 1996-703623 19960823				
US 1997-816462 19970313				
WO 1997-US14093 19970812				

PRIORITY APPLN. INFO.:

AB Protein tyrosine kinases that play a role in a no. of intracellular signal transduction processes are identified and characterized and genes encoding them are cloned. The kinases are called related adhesion focal tyrosine kinase or RAFTK. Modulation of RAFTK activity may be of use in the treatment of disease. CDNAs were cloned from megakaryocytes by PCR using degenerate primers for protein tyrosine kinases. Human and mouse cDNAs for RAFTK are very similar, indicating strong evolutionary conservation with lower levels of identity and similarity with ppl25FAK. The protein lacks transmembrane domains, myristylation sites, and SH2 and SH3 domains and interacts with protein kinase C and paxillins. Stimulation of PC-12 cells with stem cell factor changed the interaction of RAFTK with protein kinase C from via the .delta.-subunit to via the .alpha.-subunit.

AB Protein tyrosine kinases that play a role in a no. of intracellular signal transduction processes are identified and characterized and genes encoding them are cloned. The kinases are called related adhesion focal tyrosine kinase or RAFTK. Modulation of RAFTK activity may be of use in the treatment of disease. CDNAs were cloned from megakaryocytes by PCR using degenerate primers for protein tyrosine kinases. Human and mouse cDNAs for RAFTK are very similar, indicating strong evolutionary conservation with lower levels of identity and similarity with ppl25FAK. The protein lacks transmembrane domains, myristylation sites, and SH2 and SH3 domains and interacts with protein kinase C and paxillins. Stimulation of PC-12 cells with stem cell factor changed the interaction of RAFTK with protein kinase C from via the .delta.-subunit to via the .alpha.-subunit.

IT TCR (T cell receptors)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(RAFTK and signal transduction by: bprRAFTK (related adhesion focal tyrosine kinase) mols. involved in regulation of cellular processes and genes encoding them)

L2 ANSWER 6 OF 17 MEDLINE DUPLICATE 5

ACCESSION NUMBER: 97390715 MEDLINE
DOCUMENT NUMBER: 97390715
TITLE: An amphibian CD3 homologue of the mammalian CD3 gamma and delta genes.
AUTHOR: Dzialo R C; Cooper M D
CORPORATE SOURCE: Department of Medicine, University of Alabama at Birmingham 35294-3300, USA.
CONTRACT NUMBER: A130879 (NIAID)
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1997 Jul) 27 (7) 1640-7.
JOURNAL code: EN5. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
JOURNAL; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
OTHER SOURCE: GENBANK-M59925; GENBANK-X01451; GENBANK-X52993;
GENBANK-X53430; GENBANK-M12728; GENBANK-X52994;
GENBANK-X04145; GENBANK-Y00635; GENBANK-U78290;
GENBANK-Y12326
ENTRY MONTH: 199710
ENTRY WEEK: 19971005

AB T cell receptor (TCR) genes have been identified in representatives of both cartilaginous and bony vertebrates. The CD3 chains that serve as signal transducing elements of the TCR complex in mammals have been defined to a limited extent in birds. In these studies a CD3 homologue was identified in an amphibian representative, *Xenopus laevis*, using degenerate oligomer primers designed from conserved regions of avian and mammalian CD3 gamma/delta subunits. The reverse transcriptase polymerase chain reaction amplified product of *Xenopus* splenocyte RNA was then used to isolate full-length cDNA clones from a splenic library. When employed as probes, the cDNA clones hybridized with a 1-kb mRNA transcript in *Xenopus* T cells, but not in other cell types. Comparison of the deduced amino acid sequence indicated

a similar degree of homology with mammalian and avian CD3 gamma and delta chains. Genomic analysis indicated that the Xenopus CD3 molecule is encoded by five exons, a structure resembling the mammalian CD3 delta gene rather than the seven exon CD3 gamma gene. Southern blot analysis and sequencing of the 5' flanking region failed to yield evidence of a related Xenopus gene. This amphibian CD3 gene thus appears to represent an ancestral form of the mammalian CD3 gamma and delta genes.

AB T cell receptor (TCR) genes have been identified in representatives of both cartilaginous and bony vertebrates. The CD3 chains that serve as signal transducing elements of the TCR complex in mammals have been defined to a limited extent in birds. In these studies a CD3 homologue was identified in an amphibian representative, *Xenopus laevis*, using **degenerate** oligomer primers designed from conserved regions of avian and mammalian CD3 gamma/delta subunits. The reverse transcriptase polymerase chain reaction amplified product of.

L2 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1997:733370 CAPLUS

DOCUMENT NUMBER: 128:44336

TITLE: Human T cell receptor alpha and beta chain cDNA amplification with a consensus primer

AUTHOR(S): Moonka, Dilip K.; Loh, Elwyn Y.
CORPORATE SOURCE: Department Medicine, Division Gastrointestinal Diseases, University Pennsylvania Medical Center

SOURCE: Cancer Center, Philadelphia, PA, USA
Antigen T Cell Recept. (1997), 238-265. Editor(s): Oksenberg, Jorge R. Landes: Austin, Tex.
CODEN: 65HEAM

DOCUMENT TYPE: Conference

LANGUAGE: English

AB The detn. of the variable and joining sequences of T cell receptors in different human T cell populations is of interest in many biol. contexts. The use of reverse transcriptase to synthesize cDNA from mRNA followed by PCR has greatly facilitated this effort. However, the presence of variable regions presents and obvious obstacle to making specific primers for the 5' end. This work describes a **degenerate**, consensus primer that binds to a relatively conserved area of the human .alpha. and .beta. TCR variable region.

AB The detn. of the variable and joining sequences of T cell receptors in different human T cell populations is of interest in many biol. contexts. The use of reverse transcriptase to synthesize cDNA from mRNA followed by PCR has greatly facilitated this effort. However, the presence of variable regions presents and obvious obstacle to making specific primers for the 5' end. This work describes a **degenerate**, consensus primer that binds to a relatively conserved area of the human .alpha. and .beta. TCR variable region.

ST human TCR cDNA RT PCR primer

IT Genes (animal)

RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)

(Tcr; human T cell receptor alpha and beta chain cDNA amplification with a consensus primer)

IT TCR (T cell receptors)

RL: BSU (Biological study, unclassified); BIOL (Biological study) (.alpha. and .beta. chains; human T cell receptor alpha and beta chain cDNA amplification with a consensus primer)

L2 ANSWER 8 OF 17 MEDLINE

ACCESSION NUMBER: 97205328 MEDLINE

DOCUMENT NUMBER: 97205328

TITLE: alpha, beta, gamma, and delta T cell antigen receptor genes arose early in vertebrate phylogeny.

AUTHOR: Rast J P; Anderson M K; Strong S J; Luer C; Litman R T; Litman G W

CORPORATE SOURCE: Department of Pediatrics, University of South Florida, All Children's Hospital, St. Petersburg 33701, USA.

CONTRACT NUMBER: R37 AI23338 (NIAID)

SOURCE: IMMUNITY, (1997 Jan) 6 (1) 1-11.
Journal code: CCF. ISSN: 1074-7613.

PUB. COUNTRY: United States

LANGUAGE: Journal; Article; (JOURNAL ARTICLE)

FILE SEGMENT: English

OTHER SOURCE: Priority Journals

GENBANK-U75747; GENBANK-U75748; GENBANK-U75749;
GENBANK-U75750; GENBANK-U75751; GENBANK-U75752;
GENBANK-U75753; GENBANK-U75754; GENBANK-U75755;
GENBANK-U75756; GENBANK-U75757; GENBANK-U75758;
GENBANK-U75759; GENBANK-U75760; GENBANK-U75761;
GENBANK-U75762; GENBANK-U75763; GENBANK-U75764;
GENBANK-U75765; GENBANK-U75766; GENBANK-U75767;
GENBANK-U75768; GENBANK-U75769; GENBANK-U75770;
GENBANK-U75771; GENBANK-U75772; GENBANK-U75773;
GENBANK-U75774; GENBANK-U75775; GENBANK-U75776; +

ENTRY MONTH: 199706

ENTRY WEEK: 19970601

AB A series of products were amplified using a PCR strategy based on short minimally **degenerate** primers and *R. eglanteria* (clearnose skate) spleen cDNA as template. These products were used as probes to select corresponding cDNAs from a spleen cDNA library. The cDNA sequences exhibit significant identity with prototypic (alpha, beta, gamma, and delta T cell antigen receptor (TCR) genes. Characterization of cDNAs reveals extensive variable region diversity, putative diversity segments, and varying degrees of junctional diversification. This demonstrates expression of both alpha/beta and gamma/delta TCR genes at an early level of vertebrate phylogeny and indicates that the three major known classes of rearranging antigen receptors were present in the common ancestor of the present-day jawed vertebrates.

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L2 ANSWER 9 OF 17 MEDLINE
 ACCESSION NUMBER: 96068761 MEDLINE
 DOCUMENT NUMBER: 96068761
 TITLE: Analysis of rearranged T-cell receptor beta-chain genes by polymerase chain reaction (PCR) DNA sequencing and automated high resolution PCR fragment analysis.
 AUTHOR: Kneba M; Bolz I; Linke B; Hiddemann W
 CORPORATE SOURCE: Department of Internal Medicine, Georg-August University, Goettingen, Germany.
 SOURCE: BLOOD, (1995 Nov 15) 86 (10) 3930-7.
 PUB. COUNTRY: Journal code: A8G. ISSN: 0006-4971.
 LANGUAGE: English
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
 ENTRY MONTH: 199602

DUPLICATE 7

AB Polymerase chain reaction (PCR)-directed amplification and sequencing of rearranged immune genes for identification of clone-specific markers are increasingly being used in acute lymphoblastic leukemia (ALL) and non-Hodgkin's lymphoma (NHL) patients instead of the time consuming and labor intensive Southern analysis. In previous reports, no single common V beta and J beta sequence had been identified that allowed reliable amplification of the majority of rearranged T-cell antigen receptor (TCR)-beta V-D-J junctions at the DNA level because of the relatively large number of possible TCR-beta variable (V beta) and joining (J beta) gene segments involved in the rearrangement processes. In the present study we designed highly **degenerate** PCR primers directed against conserved sequences of the J beta genes. IN combination with a previously published consensus V beta primer, these J beta primers specifically amplify TCR- beta V-N(D)N-J junctions from genomic DNA. Using this approach we studied DNA extracted from biopsy material of nine patients with T-cell lymphoproliferative disorders, one c-ALL patient, and five patients with nonmalignant diseases. T-cell lines Molt 3, Jurkat, and HM 2 served as monoclonal controls. Individual PCR products were sequenced after cloning. The nucleotide sequences of 96 randomly chosen recombinant vectors were determined. In the polyclonal controls all analyzed clones differed in their TCR-beta V-N(D)N-J junctions. In the T-cell lines, in all of the T-cell malignancies, and in the c-ALL, monoclonal PCR products could be identified by demonstration of clonally restricted V-N(D)N-J junctions. The PCR results were confirmed by automated fluorescence quantification and size determination of PCR products after separation in a high-resolution polyacrylamide gel. The procedure allows rapid and specific characterization of clonal TCR-beta rearrangements from genomic DNA and will significantly simplify current experimental approaches to identify and to quantitate malignant T cells during initial staging and follow-up of T-lineage NHL and ALL patients.

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L2 ANSWER 10 OF 17 MEDLINE
 ACCESSION NUMBER: 95369847 MEDLINE
 DOCUMENT NUMBER: 95369847
 TITLE: Identification and characterization of T-cell antigen receptor-related genes in phylogenetically diverse vertebrate species.
 AUTHOR: Rast J P; Haire R N; Litman R T; Pross S; Litman G W
 CORPORATE SOURCE: University of South Florida, All Children's Hospital, St. Petersburg 33701, USA.
 CONTRACT NUMBER: R01AI23338 (NIAID)
 SOURCE: IMMUNOGENETICS, (1995) 42 (3) 204-12.
 PUB. COUNTRY: Journal code: GI4. ISSN: 0093-7711.
 LANGUAGE: English
 FILE SEGMENT: Priority Journals; Cancer Journals
 OTHER SOURCE: GENBANK-U22666; GENBANK-U22667; GENBANK-U22668; GENBANK-U22669; GENBANK-U22670; GENBANK-U22671; GENBANK-U22672; GENBANK-U22673; GENBANK-U22674; GENBANK-U22675; GENBANK-U22676; GENBANK-U22677; GENBANK-U22678; GENBANK-U22679; GENBANK-U23067
 ENTRY MONTH: 199511

DUPLICATE 8

AB Characterization of the structure, multiplicity, organization, and cell lineage-specific expression of T-cell receptor (TCR) genes of nonmammalian vertebrate species is central to the understanding of the evolutionary origins of rearranging genes of the vertebrate immune system. We recently described a polymerase chain reaction (PCR) strategy that relies on short sequence similarities shared by nearly all vertebrate TCR and immunoglobulin (Ig) variable (V) regions and have used this approach to isolate a TCR beta (TCRB) homolog from a cartilaginous fish. Using these short PCR products as probes in spleen cDNA and genomic libraries, we were able to isolate a variety of unique TCR and TCR-like genes. Here we report the identification and characterization of a chicken TCR gamma (TCRG) homolog, apparent Xenopus and pufferfish TCR alpha (TCRA) homologs, and two horned shark TCR delta (TCRD)-like genes. In addition, we have identified what could be a novel representative of the Ig gene superfamily in the pufferfish. This method of using short, minimally **degenerate** PCR primers should speed progress in the phylogenetic investigations of the TCR and related genes and lend important insights into both the origins and functions of these unique gene systems.

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L2 ANSWER 11 OF 17 MEDLINE
 ACCESSION NUMBER: 95369845 MEDLINE
 DOCUMENT NUMBER: 95369845
 TITLE: The recombination activation gene 1 (RAG1) of rainbow trout (Oncorhynchus mykiss): cloning, expression, and phylogenetic analysis.
 AUTHOR: Hansen J D; Kaattari S L
 CORPORATE SOURCE: Department of Microbiology, Oregon State University, Corvallis 97331-3804, USA..
 CONTRACT NUMBER: ES05783 (NIEHS)
 SOURCE: IMMUNOGENETICS, (1995) 42 (3) 188-95.
 PUB. COUNTRY: United States
 LANGUAGE: English
 FILE SEGMENT: Priority Journals; Cancer Journals
 OTHER SOURCE: GENBANK-U19663
 ENTRY MONTH: 199511

DUPLICATE 9

AB The characterization of genes involved in the generation of the immune repertoire is an active area of research in lower vertebrate taxa. The recombination activating genes (RAG) have been shown to be essential for V (D) J recombination of T-cell antigen receptor (TCR) and immunoglobulin (Ig) genes, leading to the generation of the primary repertoire. As RAG1 is critical to the differentiation of pre-B and -T cells, its expression within an associated primary lymphoid organ can serve as a developmental marker. To examine the ontogeny of lymphocytes in *Oncorhynchus mykiss*, we cloned RAG1 from trout and examined its tissue- and lymphocyte-specific expression. The polymerase chain reaction, coupled with degenerate oligonucleotide primers, was used to amplify a homologous probe [(633 base pairs) (bp)] from rainbow trout genomic DNA, which in turn was used to isolate a lambda genomic clone. Sequence analysis of this genomic clone confirmed the RAG1 nature of this gene (3888 bp) and revealed an internal intron of 666 bp. When compared with other previously reported RAG1 sequences, the predicted amino acid translation (1073 aa) displayed a minimum of 78% similarity for the complete sequence and 89% similarity in the conserved region (aa 417-1042). Using northern blot analysis, we found the expression of RAG1 to be limited to surface Ig-n lymphocytes within the thymus. This data forms the basis for a proposal that the thymus of teleost species plays an essential developmental role in lymphopoiesis and thus can be regarded as a primary lymphoid organ.

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L2 ANSWER 12 OF 17 MEDLINE
 ACCESSION NUMBER: 95252184 MEDLINE
 DOCUMENT NUMBER: 95252184
 TITLE: Cloning the rat homolog of the CD28/CTLA-4-ligand B7-1: structural and functional analysis.
 AUTHOR: Judge T A; Liu M; Christensen P J; Fak J J; Turka L A
 CORPORATE SOURCE: Department of Internal Medicine, University of Michigan Medical School, Ann Arbor 48109, USA..
 CONTRACT NUMBER: MO1RR00042 (NCRR)
 SOURCE: INTERNATIONAL IMMUNOLOGY, (1995 Feb) 7 (2) 171-8.
 PUB. COUNTRY: ENGLAND: United Kingdom
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 OTHER SOURCE: GENBANK-U05593
 ENTRY MONTH: 199508

DUPLICATE 10

AB T cell activation involves the delivery of two independent signals to the naive T cell. The first signal occurs with engagement of the TCR . . . One of the best characterized second signals is ligation of CD28 on the surface of T cells by B7 molecules (B7-1, B7-2) present on the surface of activated antigen presenting cells (APCs). Recent studies have demonstrated that injection of a human fusion protein, CTLA-4-Ig, which in humans binds to both B7-1 and B7-2, prevents cardiac allograft rejection in a rat transplantation model when given 48 h after engraftment. In order to better characterize the role of B7-1 (which is maximally expressed 48 h after activation of APCs) in this model, as well as in models of tumor-induced immune responses, we have cloned the rat homolog of B7-1, and now report on its structure and function. A 1030 bp cDNA containing the entire coding sequence of the rat B7-1 was cloned with a polymerase chain reaction strategy utilizing degenerate primers derived from published murine and human B7-1 sequences. The rat B7-1 coding sequence is 67 and 81% homologous to human and murine B7-1 cDNAs, and the predicted peptide sequence is likewise 57 and 66% identical to the peptide sequences of human and murine B7-1 respectively. The greatest area of identity occurs in the extracellular portion of the molecule, particularly the Ig-C like domain. (ABSTRACT TRUNCATED AT 250 WORDS)
 AB . . . involves the delivery of two independent signals to the naive T cell. The first signal occurs with engagement of the TCR. One of

the best characterized second signals in regulation of CD28 on the surface of T cells by B7 molecules. . . bp cDNA containing the entire coding sequence of the rat B7-1 was cloned with a polymerase chain reaction strategy utilizing **degenerate primers** derived from published murine and human B7-1 sequences. The rat B7-1 coding sequence is 67 and 81% homologous to human.

L2 ANSWER 13 OF 17 MEDLINE
 ACCESSION NUMBER: 95023888 MEDLINE
 DOCUMENT NUMBER: 95023888
 TITLE: T-cell receptor gene homologs are present in the most primitive jawed vertebrates.
 AUTHOR: Rast J P; Litman G W
 CORPORATE SOURCE: Department of Pediatrics, University of South Florida, All Children's Hospital, St. Petersburg 33701..
 CONTRACT NUMBER: AI-23338 (NIAID)
 SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1994 Sep 27) 91 (20) 9248-52. Journal code: PV3. ISSN: 0027-8424.
 PUB. COUNTRY: United States
 LANGUAGE: English
 FILE SEGMENT: Cancer Journals; Priority Journals
 OTHER SOURCE: GENBANK-U07622; GENBANK-U07623; GENBANK-U07624; GENBANK-U09531; GENBANK-U09532; GENBANK-U09533; GENBANK-U09534
 ENTRY MONTH: 199501

DUPLICATE 11

AB The phylogenetic origins of T-cell immunity and T-cell antigen receptor (TCR) genes have not been established. A PCR approach using short, minimally **degenerate** oligodeoxynucleotide primers complementing conserved variable region segments amplifies TCR -like products from the genomic DNA of *Heterodontus francisci* (horned shark), a representative phylogenetically primitive cartilaginous fish. One of these products has been used as a probe to screen a *Heterodontus* spleen cDNA library and a clone was identified that is most related at the nucleotide sequence and predicted peptide levels to higher vertebrate TCR beta-chain genes. Genomic analyses of the TCR homologs indicate that recombining variable and joining region segments as well as constant region exons are encoded by extensive gene families, organized in the multicluster form, characteristic of both the immunoglobulin heavy- and light-chain gene loci in the cartilaginous fishes. Greater numbers of homologous products were identified when a probe complementing the putative constant region of the TCR homolog was used to screen the same cDNA library. A high degree of intergenic variation is associated with the putative variable region segments of these isolates. Direct evidence is presented for TCR -like genes, which presumably are associated with T-cell function, at the earliest stages in the phylogenetic emergence of jawed vertebrates.

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L2 ANSWER 14 OF 17 MEDLINE
 ACCESSION NUMBER: 94179857 MEDLINE
 DOCUMENT NUMBER: 94179857
 TITLE: A consensus primer to amplify both alpha and beta chains of the human T cell receptor.
 AUTHOR: Moonka D; Loh E Y
 CORPORATE SOURCE: Department of Medicine, University of Pennsylvania Medical Center, Philadelphia..
 CONTRACT NUMBER: AI33214 (NIAID)
 SOURCE: JOURNAL OF IMMUNOLOGICAL METHODS, (1994 Feb 28) 169 (1) 41-51. Journal code: IFE. ISSN: 0022-1759.
 PUB. COUNTRY: Netherlands
 LANGUAGE: English
 FILE SEGMENT: Priority Journals; Cancer Journals
 ENTRY MONTH: 199406

DUPLICATE 12

AB The use of reverse transcriptase in conjunction with the polymerase chain reaction (RT-PCR) has proven invaluable in the analysis of the T cell receptor (TCR) repertoire of different populations of T cells. However, the presence of a variable region in the T cell receptor has hindered the design of primers for the 5' end of the TCR cDNA. We describe the design and use of a **degenerate** consensus primer that allows amplification of both the alpha and beta chains of the human TCR. We have used this primer in the analysis of the TCR distribution of T cell clones, peripheral blood lymphocytes and lymphocytes residing in tissue. In addition, the primer has allowed the identification of an alternative splice site in the beta chain constant region which cannot translate into a functional constant region. We have found the primer to be easy to use, sensitive and specific.

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L2 ANSWER 15 OF 17 MEDLINE

DUPLICATE 13

ACCESSION NUMBER: 94014793 MEDLINE
 DOCUMENT NUMBER: 94014793
 TITLE: Ex vivo clonotype primer-directed gene amplification to identify malignant T cell repertoires.
 AUTHOR: Beers T; Du T L; Rickert M; Overturf P; Choi Y; Greenberg S J
 CORPORATE SOURCE: Department of Neurology, Roswell Park Cancer Institute, Buffalo, NY 14263.
 SOURCE: JOURNAL OF LEUKOCYTE BIOLOGY, (1993 Oct) 54 (4) 343-50. Journal code: IWY. ISSN: 0741-5400.
 PUB. COUNTRY: United States
 LANGUAGE: Journal; Article; (JOURNAL ARTICLE)
 FILE SEGMENT: English
 ENTRY MONTH: Priority Journals; Cancer Journals
 ENTRY MONTH: 199401

AB A novel strategy that utilizes input genomic DNA and overcomes limitations encountered with traditional RNA reverse transcription-polymerase chain reaction (PCR) amplification methodology is described to screen for T cell receptor (TCR) repertoires. The methodology has been developed to identify individual T cell clonotypes with regard to their unique receptor beta chain variable/diversity/joining (VDJ) region gene rearrangement. The technique avoids preselection for a given antigen specificity and is therefore independent of artificial bias introduced by in vitro cell population expansion. This technique was used to detect and identify genetically of malignant clones from heterogeneous mononuclear cell populations from an array of hemato-oncological disorders, including mycosis fungoides/Sézary Syndrome, adult T cell leukemia, and large granular lymphoproliferative disease. An initial primary PCR, directed by a TCR-J beta generic primer and a complement of family-specific TCR-V beta primers, defines predominant T cell receptor variable gene usage. Use of a TCR-J beta generic primer supplants the use of a constant region primer anchor and thus eliminates the need to target mRNA. The process of variable gene screening also expedites gene sequencing. By sequencing through the VDJ juxtaposed region, i.e., the third complementarity determinant region, clonotype-specific primers are developed and used in a secondary clonotype primer-directed PCR (CPD-PCR) to detect, with extreme sensitivity and specificity, unique T cell clonal repertoires. Analysis of the products of the CPD-PCR permits the detection of a single malignant cell among one million polyclonal cells and supercedes the constraints of prior studies that provide a limited evaluation of family variable gene repertoire usage. This strategy may be applied in the detection of minimal residual disease, in surveillance after induction of disease-free states, and in analyzing the effectiveness of purging autologous bone marrow of malignant clones.

AB . . . limitations encountered with traditional RNA reverse transcription-polymerase chain reaction (PCR) amplification methodology is described to screen for T cell receptor (TCR) repertoires. The methodology has been developed to identify individual T cell clonotypes with regard to their unique receptor beta chain. . . including mycosis fungoides/Sézary Syndrome, adult T cell leukemia, and large granular lymphoproliferative disease. An initial primary PCR, directed by a TCR-J beta generic primer and a complement of family-specific TCR-V beta primers, defines predominant T cell receptor variable gene usage. Use of a TCR-J beta generic primer supplants the use of a constant region primer anchor and thus eliminates the need to target mRNA. The process of.

L2 ANSWER 16 OF 17 MEDLINE
 ACCESSION NUMBER: 91184261 MEDLINE
 DOCUMENT NUMBER: 91184261
 TITLE: Conserved nucleotide sequences at the 5' end of T cell receptor variable genes facilitate polymerase chain reaction amplification.
 AUTHOR: Broeren C P; Verjans G M; Van Eden W; Kusters J G; Lenstra J A; Logtenberg T
 CORPORATE SOURCE: Institute of Infectious Diseases and Immunology, School of Veterinary Medicine, University of Utrecht, The Netherlands.
 SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1991 Mar) 21 (3) 569-75. Journal code: EN5. ISSN: 0014-2980.
 PUB. COUNTRY: GERMANY: Germany, Federal Republic of
 LANGUAGE: Journal; Article; (JOURNAL ARTICLE)
 FILE SEGMENT: English
 ENTRY MONTH: Priority Journals; Cancer Journals
 ENTRY MONTH: 199107

DUPLICATE 14

AB Alignment of all available nucleotide sequences of mouse and rat alpha/beta T cell receptor (TcR) variable (V) regions revealed the presence of relatively conserved sequences at the 5' end of the V gene segments. Based on these conserved sequences, degenerate primers were developed for use in the polymerase chain reaction (PCR). The degenerate primers developed on the basis of the conserved sequences at the 5' end of rat and mouse V gene segments are expected to enable the amplification of all mouse and rat TcR alpha/beta chain V regions. To test their applicability, the primers were used for the amplification of the V region of the TcR alpha/beta expressed by rat T cell lines. After amplification, the TcR V regions expressed were cloned and sequenced. The Z1a T cell line was shown to use the same TcR V gene segments (V alpha 2 and V beta 8.2), as most other experimental allergic encephalomyelitis associated T cell lines, but had different D and J segments. In spite of these differences at the nucleotide level, a remarkable conservation of the amino acid sequence at the V beta D beta J beta junction was found. Alignment of a large number of human V alpha and V beta gene segments revealed the presence of similarly conserved sequences. Degenerate primers based on these conserved sequences enabled the amplification of TcR V regions of human T cell lines.

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lines, . . . of a large number of human . . . alpha and V beta gene segments revealed the presence of similarly conserved sequences. **Degenerate primers** based on these conserved sequences enabled the amplification of Tcr V regions of human T cell lines.

L2 ANSWER 17 OF 17 MEDLINE
ACCESSION NUMBER: 90293689 MEDLINE DUPLICATE 15
DOCUMENT NUMBER: 90293689
TITLE: The presumptive CDR3 regions of both T cell receptor alpha and beta chains determine T cell specificity for myoglobin peptides.
AUTHOR: Danska J S; Livingstone A M; Paragas V; Ishihara T; Fathman C G
CORPORATE SOURCE: Department of Medicine, Stanford University School of Medicine, California 94305..
CONTRACT NUMBER: AI-19512 (NIAID)
AI-27989 (NIAID)
DK-39959 (NIDDK)
+
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1990 Jul 1) 172 (1) 27-33.
Journal code: I2V. ISSN: 0022-1007.
PUB. COUNTRY: United States
LANGUAGE: Journal; Article; (JOURNAL ARTICLE)
English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199010

AB The T cell receptor alpha/beta (TCR-alpha/beta) is encoded by variable (V), diversity (D), joining (J), and constant (C) segments assembled by recombination during thymocyte maturation to produce a heterodimer that imparts antigenic specificity to the T cell. Unlike immunoglobulins (Igs), which bind free antigen, the ligands of TCR-alpha/beta are cell surface complexes of intracellularly degraded antigens (i.e., peptides) bound to and presented by polymorphic products of the major histocompatibility complex (MHC). Therefore, antigen recognition by T cells is defined as MHC restricted. A model has been formulated based upon the similarity between TCR-alpha/beta V region and Ig Fab amino acid sequences, and the crystal structure of the MHC class I and Ig molecules. This model predicts that the complementarity determining regions (CDR) 1 and 2, composed of TCR V alpha and V beta segments, primarily contact residues of the MHC alpha helices, whereas V/J alpha and V/D/J beta junctional regions (the CDR3 equivalent) contact the peptide in the MHC binding groove. Because polymorphism in MHC proteins is limited relative to the enormous diversity of antigenic peptides, the TCR may have evolved to position the highly diverse junctional residues (CDR3), where they have maximal contact with antigen bound in the MHC peptide groove. Here, we demonstrate a definitive association between CDR3 sequences in both TCR alpha and beta chains, and differences in recognition of antigen fine specificity using a panel of I-Ed-restricted, myoglobin-reactive T cell clones. Acquisition of these data relied in part upon a modification of the polymerase chain reaction that uses a **degenerate**, consensus primer to amplify TCR alpha chains without foreknowledge of the V alpha segments they utilize.

AB The T cell receptor alpha/beta (TCR-alpha/beta) is encoded by variable (V), diversity (D), joining (J), and constant (C) segments assembled by recombination during thymocyte maturation to . . . a heterodimer that imparts antigenic specificity to the T cell. Unlike immunoglobulins (Igs), which bind free antigen, the ligands of TCR-alpha/beta are cell surface complexes of intracellularly degraded antigens (i.e., peptides) bound to and presented by polymorphic products of the major . . . antigen recognition by T cells is defined as MHC restricted. A model has been formulated based upon the similarity between TCR-alpha/beta V region and Ig Fab amino acid sequences, and the crystal structure of the MHC class I and Ig molecules. This model predicts that the complementarity determining regions (CDR) 1 and 2, composed of TCR V alpha and V beta segments, primarily contact residues of the MHC alpha helices, whereas V/J alpha and V/D/J beta . . . the MHC binding groove. Because polymorphism in MHC proteins is limited relative to the enormous diversity of antigenic peptides, the TCR may have evolved to position the highly diverse junctional residues (CDR3), where they have maximal contact with antigen bound in the MHC peptide groove. Here, we demonstrate a definitive association between CDR3 sequences in both TCR alpha and beta chains, and differences in recognition of antigen fine specificity using a panel of I-Ed-restricted, myoglobin-reactive T cell clones. Acquisition of these data relied in part upon a modification of the polymerase chain reaction that uses a **degenerate**, consensus primer to amplify TCR alpha chains without foreknowledge of the V alpha segments they utilize.

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